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ABSTRACT

The Committee on Education Programs in Laboratory Animal Science (EPLAS) has prepared this guide to aid institutions in implementing an education and training program that will meet the expectations of the Public Health Service (PHS). This guide was designed to fulfill several purposes. First, it is intended to assist institutional officials and institutional animal care and use committees (IACUCs) in determining the scope and depth of education training programs that will meet both institutional needs and the requirements of the PHS. Second, it is offered as a reference for the person or committee assigned the responsibility for coordinating these programs. Finally, portions of the guide will be useful to those people (content experts) who develop the material to be presented. To accommodate the diverse backgrounds and needs of personnel, the committee has developed a multiphase program. Those topics considered essential elements for all personnel have been arranged into a single introductory module. The next three modules cover specific species, pain-management, and surgery. The next section of the guide contains detailed content outlines of the subjects covered in the four modules. The material in the modules is cross-referenced to appropriate subtopics in this section. Information on the following topics is provided: (1) laws, regulations, and policies that impact on the care and use of animals; (2) ethical and scientific issues; (3) alternatives to dissection; (4) responsibilities of the institution, the animal care and use committee, and the research and veterinary staffs; (5) pain and distress; (6) anesthetics, tranquilizers, analgesics, and neuromuscular blocking agents; (7) survival surgery and postsurgical care; (8) euthanasia; (9) husbandry, care, and the importance of the environment; and (10) a species-specific overview. The next section contains sources of information, selected bibliography, and audiovisual materials. The last section provides information on how to develop, deliver, and evaluate an educational program. Principles for the utilization and care of vertebrate animals used in testing, research, and training; a description of the Animal Welfare Information Center; and samples of learning objectives or self-assessment statements that coordinators may want to use or adapt for use at their institutions are appended. (KR)

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Education and Training in the Care and Use of Laboratory Animals

A Guide for Developing Institutional Programs

Committee on Educational Programs in Laboratory Animal Science
Institute of Laboratory Animal Resources
Commission on Life Sciences
National Research Council

NATIONAL ACADEMY PRESS
Washington, D.C. 1991

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, National Academy of Engineering, and Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, National Academy of Engineering, and Institute of Medicine.

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The Institute of Laboratory Animal Resources (ILAR) was founded in 1952 under the auspices of the National Research Council. Its mission is to provide expert counsel to the federal government, the biomedical research community, and the public on the scientific, technological, and ethical use of laboratory animals within the context of the interests and mission of the National Academy of Sciences. ILAR promotes the high-quality, humane care of laboratory animals; the appropriate use of laboratory animals; and the exploration of alternatives in research, testing, and teaching.

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Preface

The Committee on Educational Programs in Laboratory Animal Science was appointed in 1988 to "prepare an annotated syllabus [guide] for a course in humane practices of animal care and use to assist institutions in complying with recently enacted federal laws, which mandate that educational programs be provided for personnel who use animals in research, testing, and teaching." The committee met four times between November 1988 and June 1990. During the first meeting, several decisions were made that determined the scope and content of this report. First, to assist the scientific community in meeting its demonstrated commitment to humanely care for and use research animals, it was determined that the report would include more information and in much more depth than is necessary to meet minimal requirements of existing regulations. Second, it was resolved that the intended audience should be anyone who can directly or indirectly influence the well-being of animals. These people include investigators, research technicians, teachers, teaching assistants, people in physical plant maintenance, and administrators and animal care staff, all of whom need an understanding of their responsibilities to make an institution's animal care and use program successful. It was also decided that the report would address primarily the principal species used in biomedical research, with limited inclusion of less commonly used species. The care and use of animals in agricultural research were considered beyond the scope of the committee's charge. The consensus was that the committee would develop a core syllabus appropriate for every institution where animal research is performed. In addition, a number of individual packages would be developed that would allow each institution to adapt this guide to its own unique needs. It was recognized that many of the research facilities that will use this guide are not academic institutions and that some basic guidance on development, presentation, and evaluation of an education and training program should be included.

The committee recognizes that this report reflects only an initial effort to fulfill both the scientific community's need for information and the mandated requirements for education and training in the care and use of laboratory animals. The dynamics of biomedical research and legislation, critical comments by those who use the guide, and the ongoing development of audiovisual programs will almost certainly require that the report be extensively revised within a few years. The committee hopes that this guide serves as the first building stone in the development of institutional education and training programs that assist scientists in the conduct of biomedical research, as well as meeting the spirit and intent of federal legislation.

The committee extends its appreciation to Kevin P. Engler and Jean A. Larson of the National Agricultural Library's Animal Welfare Information Center, who prepared the appendix on how to use the center, and to the staff of the Institute of Laboratory Animal Resources, especially Dorothy D. Greenhouse, whose support has made this document possible.

Gale D. Taylor, Chairman
Committee on Educational Programs in
Laboratory Animal Science

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I
INTRODUCTION

1

Introduction

In 1985, Congress enacted two laws containing provisions concerning the care and use of animals in research, testing, and education: the Health Research Extension Act (Public Law 99-158) and the Food Security Act (Public Law 99-198). The former revised the Public Health Service Act (42 U.S.C. 289d) and made compliance with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals a matter of law for all PHS-funded research. The latter extensively amended the Animal Welfare Act (7 U.S.C. 2131-2156). Both laws contain a requirement that institutions provide training for staff who care for or use animals. The regulations that implement the Animal Welfare Act specifically require that institutions provide training in:

- A. Humane methods of animal maintenance and experimentation, including:
 - 1. basic needs of each species of animal maintained at the institution;
 - 2. proper handling and care for various species of animals used by the facility;
 - 3. proper preprocedural and postprocedural care of animals; and
 - 4. aseptic surgical methods and procedures.
- B. The concept, availability, and use of research or testing methods that limit the use of animals or minimize animal distress;
- C. Proper use of anesthetics, analgesics, and tranquilizers for any species of animals used by the facility;
- D. Methods whereby deficiencies in animal care and treatment are reported, including deficiencies in animal care and treatment reported by any employee of the facility.
- E. Utilization of services available to provide information:
 - 1. on appropriate methods of animal care and use;
 - 2. on alternatives to the use of live animals in research;

3. that could prevent unintended and unnecessary duplication of research involving animals; and
4. regarding the intent and requirements of the Act.

PHS policy requires that PHS-funded institutions file an Animal Welfare Assurance that must include "a synopsis of training or instruction in the humane practice of animal care and use, as well as training or instruction in research or testing methods that minimize the number of animals required to obtain valid results and minimize animal distress, offered to scientists, animal technicians, and other personnel involved in animal care, treatment, or use" (PHS, 1986, p. 4).

The Committee on Educational Programs in Laboratory Animal Science (EPLAS) has prepared this guide to aid institutions in implementing an education and training program that will meet the expectations of the PHS Office for Protection from Research Risks (OPRR), which oversees the PHS policy, and the Regulatory Enforcement and Animal Care (REAC) unit of the Animal and Plant Health Inspection Service, U.S. Department of Agriculture, which regulates the Animal Welfare Act. This guide has been designed to fulfill several purposes. First, it is intended to assist institutional officials and institutional animal care and use committees (IACUCs) in determining the scope and depth of education and training programs that will meet both institutional needs and the requirements of the OPRR and REAC. Second, it is offered as a reference for the person or committee assigned the responsibility for coordinating these programs. Finally, portions of the guide will be useful to those people (content experts) who develop the material to be presented.

The EPLAS committee firmly believes that a strong education program on the care and use of laboratory animals goes beyond the involvement of scientists, research technicians, and animal care personnel. To promote understanding of the scientific process and minimize misunderstandings, the committee suggests that administrators, nonscientific members of IACUCs, support staff, and other nonscientific personnel indirectly involved in activities using live animals be included in the program.

To accommodate the diverse backgrounds and needs of personnel, the committee has developed a multiphase program. Those topics considered essential elements for all personnel have been arranged into a single introductory module (core module). The core module has intentionally been designed as a broad overview that can be presented in 3 to 4 hours. The overall goals are to give personnel an appreciation of the scope and intent of the laws, regulations, and policies and to facilitate compliance by providing them with pertinent information and by directing them to additional skill training and resources.

The IACUC and the course coordinator are responsible for developing clear objectives for each phase of the training program. These objectives must incorporate both federally mandated and institutional requirements. The methods for presenting the material will depend on the audience, the objectives that have been set, the nature of the content, and the resources available.

This committee recognizes that people who provide day-to-day animal care require additional training that goes beyond the scope and content proposed in this document. There is no suggestion that the program proposed in this report should in any way replace

existing programs such as those offered by the American Association for Laboratory Animal Science (AALAS).

We also recognize that the approach we have taken will require considerable time and planning by the instructional staff; however, the committee believes that the suggested program provides the necessary information without encumbering scientific personnel with hours of training in species or research techniques inappropriate to their needs. We believe the strategy we have adopted fulfills the requirements of the PHS policy and the regulations of the Animal Welfare Act, while being flexible enough to serve the needs of the wide variety of institutions that must comply with these requirements.

REFERENCE

PHS (Public Health Service). 1986. Animal welfare assurance. P. 4 in Public Health Service Policy on Humane Care and Use of Laboratory Animals. Washington, D.C.: U.S. Department of Health and Human Services. Copies available from: Office for Protection from Research Risks, Building 31, Room 4B09, National Institutes of Health, Bethesda, MD 20892

2

How to Use This Guide

To fully understand this guide, all of the introductory material in Part I should be read before proceeding to Part II. Part II contains four course modules that can be customized to fit the needs of the institution's education and training program. The first of these, the core module, is intended for all personnel involved both directly and peripherally with laboratory animals used in research, education, and testing, and for some of these people, it will satisfy the total educational requirement. The other three modules are intended for select groups of personnel according to their need to know. Species-specific sessions, with hands-on training, should be provided for all people who will be in direct contact with animals. In addition, the pain-management and surgery modules should be offered if they are applicable to the institution's needs.

These modules are hierarchical. The species-specific module builds on introductory material in the core. The pain module builds on both the core and the species-specific modules, while the surgery module requires information and skills presented in all three preceding modules. The modules furnish major topic headings and provide a cross-reference to Part III, which contains detailed outlines of the material contained in the modules. This cross-referencing indicates the depth of presentation within the module. For example, both the Core Module and the Pain-Management Module show anesthetics as a topic and refer to the content outline in chapter 6. However, the Core Module draws primarily from the first point in chapter 6 (i.e., 6.1), while the Pain-Management Module recommends covering the entire outline. Content experts asked to deliver information or teach skills should be provided with both the module outline and the corresponding content outlines from Part III. In addition to guiding the speakers, these outlines can also be used to select alternative (e.g., audiovisual, computer-aided, and independent-study) instructional

materials. Some sections might also be useful as handouts. Permission for limited reproduction of portions of this book for educational purposes, but not for sale, may be granted on receipt of a written request to the National Academy Press, 2101 Constitution Avenue, Washington, DC 20418.

Part IV lists audiovisual and computer-aided teaching materials and cites organizations that can furnish information on the topics recommended for presentation. It also includes a bibliography. The references that the committee believes are essential for a minimum institutional library have been designated by an asterisk.

The three chapters that make up Part V may be helpful to some IACUCs and course coordinators. They present very basic material on how to approach the task of education and training, how to plan and deliver a lecture-based program, and how to evaluate the institutional program and individual courses.

Three appendixes provide a set of principles adopted by the federal government for the humane care and use of animals, a description of the Animal Welfare Information Center of the National Agricultural Library, and a series of statements that can be used by course coordinators for developing learning objectives or by participants for self-assessment.

II

COURSE MODULES

1

Core Module

INTRODUCTION

The core module is recommended for all personnel involved both directly and peripherally with animals used in research, education, and testing. It has been designed as an introduction that will enable participants to follow through on subjects that relate to their interests.

A lecture/seminar format is recommended for presenting most of the core material, as this format is well suited for communicating the institutional mandate, is appropriate for groups of any size, and makes the most efficient use of resources. If the number of people requiring training within an institution is very small, consideration might be given to participation in a program offered by a larger institution or to the pooling of resources by several small institutions. A session might include several speakers, each of whom is responsible for an assigned topic. Prepackaged video or slide materials can be used effectively for portions of the presentation, particularly when human resources are limited. Handouts are also useful adjuncts to the presentation. Two of the appendixes to this guide are recommended as handouts in the outline below. It is also recommended that written institutional policies applicable to the topics be distributed. Other handouts should be developed to fit the needs of the speakers and the participants.

The topics contained in the outline below are those considered by the EPLAS committee to be essential elements of an introductory education program on the care and use of laboratory animals. The recommended presentation time is 3 to 4 hours. In this amount of time, it will not be possible to deal with the topics in depth; however, it is important to address the legal and ethical aspects of every topic. Although the committee has estimated a presentation time for each topic in the outline, the actual time will depend

on the emphasis to be placed on each topic and depth of coverage required to fulfill the needs of the institution and the participants. In addition, significant time should be allotted for participants to ask questions and discuss the issues.

The recommended content of each topic below is cross-referenced to the expanded outlines contained in Part III, Chapters 1-9, of this guide by the numbers in parentheses following each sentence. The number preceding the decimal point indicates the chapter, and the number(s) following the decimal point indicates the place within the chapter that the information appears. Thus, 1.1 indicates the first entry in chapter 1 of part III, and 1.2.1 indicates the first subentry under the second entry in chapter 1.

OUTLINE FOR THE CORE MODULE

Laws, Regulations, and Policies That Impact on the Care and Use of Animals

Estimated Presentation Time: 10-15 minutes

Recommended Handout: Written institutional policies related to the care and use of laboratory animals

- Briefly describe federal laws, regulations, and policies that have an impact on the care and use of animals (1.1).
- Describe the U.S. Department of Agriculture (USDA) and Public Health Service (PHS) methods for ensuring and monitoring compliance, including the consequences of noncompliance to the institution and the individual (1.1).
- Present in detail the composition and functions of the institutional animal care and use committee (IACUC) (1.2.1).
- Describe the records that facilities are required to keep (1.2.3).
- Describe the reports required by animal welfare regulations and PHS policy (1.2.4).
- Describe state and local laws that have an impact on the care and use of animals, if applicable (1.3).
- Present the policies of your institution (1.4).

Ethical and Scientific Issues

Estimated Presentation Time: 10-15 minutes

Recommended Handout: U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (Appendix I)

- Define ethics and applied ethics (2.1).
- Compare the utilitarian and deontological (relating to moral obligation) methods for making decisions (2.2).
- Compare the position of people who accept the use of animals in research, testing, and education with that of people who oppose such use (2.3-2.4).
- Discuss the role played by laws, regulations, and policies in ensuring humane care and use of animals (2.5).
- Present suggested ethical principles for the use of animals (2.6) and encourage participants to develop a personal code of ethics that emphasizes animal welfare.

Alternatives

Estimated Presentation: 10-15 minutes

Recommended Handouts: Reprint of The Animal Welfare Information Center, which can be found in Appendix II; list of names and telephone numbers for consulting veterinary staff, statisticians, and others

- Define the "3R's" and discuss their relevance (3.1).
- Present regulatory, ethical, humane, economic, and scientific reasons for considering alternatives (3.2).
- Provide examples of nonanimal research methods and models (3.3).
- Review statistical methods used to determine how many animals will be required for a valid experiment (3.3.8).
- Review factors that influence the selection of animal models (3.4).
- Familiarize participants with resources and services that provide information on alternatives (3.5).

Responsibilities of the Institution, the Animal Care and Use Committee, and the Research and Veterinary Staffs

Estimated Presentation Time: 25-30 minutes

- List and describe responsibilities of the institution (4.1).
- List and describe responsibilities of the IACUC (4.2).
- List and describe responsibilities of investigators (4.3).
- List and describe responsibilities of the attending veterinarian (4.4).

Pain and Distress

Estimated Presentation Time: 10-15 minutes

- Define comfort, discomfort, stress, distress, and pain (5.1).
- Discuss categories of pain (5.2).
- Discuss perception of pain and methods of assessing it in animals (5.3-5.4).
- Discuss sources of stress and the value of adaptation to the animal (5.5.1).
- Discuss sources of distress and describe signs of maladaptive behavior (5.5.2-5.6).
- Discuss the ethical and legal obligations of the scientific staff to prevent or minimize pain and distress, and describe the role of the IACUC (5.7-5.8).
- Discuss adequate veterinary care as it relates to this issue (5.9).

Anesthetics, Analgesics, Tranquilizers, and Neuromuscular Blocking Agents

Estimated Presentation Time: 20-25 minutes

- Briefly define and compare anesthetics, analgesics, tranquilizers, sedatives, and neuromuscular blocking agents, including indicators for the use of each (6.1-6.4).
- Give examples of chemical agents commonly used to achieve general anesthesia, analgesia, sedation, and immobilization (6.1-6.4).
- Present factors that modify the response of an animal to these agents (6.1.5, 6.5).

- Describe the stages of general anesthesia and present methods of determining when an animal is sufficiently anesthetized (6.1.6-6.1.7).
- Describe the indications of an anesthetic overdose and the steps necessary to overcome it (6.1.8).
- Discuss safety precautions for storing drugs and requirements for recordkeeping (6.6-6.7).
- Discuss the function of the attending veterinarian, with an emphasis on involving veterinary care staff in drug selection, administration, and monitoring (6.8).

Survival Surgery and Postsurgical Care

Estimated Presentation Time: 10-15 minutes

- Define aseptic technique, survival surgery, major survival surgery, and minor surgical procedures (7.1).
- Discuss the legal requirements related to performing surgery on animals (7.2).
- Briefly describe how the surgical team should prepare for aseptic surgery, including preparation of the animal (7.3).
- Briefly discuss complications of surgery and ways to prevent them (7.5-7.6).
- Discuss the importance of postsurgical care and the equipment needed to monitor and support the patient (7.7-7.8).
- Describe the records that should be kept (7.9).

Euthanasia

Estimated Presentation Time: 20-25 minutes

- Define euthanasia (8.1).
- Present legal requirements (8.2).
- Present ethical and humane considerations (8.3).
- Discuss the need for sensitivity when euthanasia is performed, emphasizing the public's concerns, the importance of professional conduct, and the effect euthanasia may have on personnel (8.4).
- Give an overview of pharmacologic and nonpharmacologic options, and provide criteria for selecting a method (8.5-8.7).
- Discuss health and safety measures associated with handling animal carcasses, particularly those in which the animal is known to have carried a zoonotic agent or to have been exposed to a substance hazardous to personnel (8.8).

Husbandry, Care, and the Importance of the Environment

Estimated Presentation Time: 20-25 minutes

- Discuss legal requirements for husbandry and care (9.1).
- Discuss the importance of proper husbandry and a stable environment (9.2).
- Discuss environmental variables that can be controlled, giving examples of variables that can affect animal health and research outcomes (9.3).

- Describe procedures for emergencies such as power failures (9.4).

Resources

Estimated Presentation Time: 10-15 minutes

Recommended Handout: The Animal Welfare Information Center (Appendix I)

- Discuss the services of the Animal Welfare Information Center, National Agricultural Library (Appendix I), and other resources (Part IV, section 1).
- Discuss technical services, reference texts, and audiovisual material available from the laboratory animal resources unit.
- Provide or explain the mechanism for obtaining copies of pertinent literature.

2

Species-Specific Module

INTRODUCTION

This module should be provided for all people who will be in direct contact with animals. Only one species or closely related species should be covered in a particular session. The emphasis on each topic will vary according to the needs of the participants and the species of animal considered.

The cognitive aspects of the species-specific module can be presented in the form of independent-study materials; therefore, estimated presentation times are not included. Demonstrations and visual aids should not be substituted for the hands-on experience needed by participants to develop their skills, although they can be helpful in introducing a laboratory exercise. Associated skill-building sessions should be done in small groups or in individual laboratory settings.

As in the core module, the recommended content of each topic below is cross-referenced to the expanded outlines contained in Part III. The material will be found primarily in Chapter 10 (Species-Specific Overview), with additional material taken from Chapters 8 (Euthanasia) and 9 (Husbandry, Care, and Importance of the Environment).

OUTLINE FOR THE SPECIES-SPECIFIC MODULE

Selection and Procurement of Animals

- Discuss options in selecting appropriate animals for study (10.1).

- Give sources of information on suppliers of animals (10.2.1).
- Discuss in detail any legal requirements and institutional policies that relate to procurement of animals (10.2.2).

Husbandry and Care

- Review the importance of proper husbandry and a stable environment to research (9.2).
- Describe in detail laws, regulations, and policies pertaining to husbandry and care, including environmental enrichment (9.1).
- Review controllable environmental variables (9.3).
- Describe the advantages and disadvantages of the different types of caging available in your institution (10.3.1.1).
- Present acceptable population densities for various types of caging and the effects of overcrowding (10.3.1.2).
- Discuss the use of special caging (10.3.2).
- Describe available methods of environmental enrichment (10.4).
- Describe food- and water-delivery methods and diets available in your institution, including information on administering experimental agents in food or water and carrying out approved studies involving food or water deprivation (10.5-10.6).

Handling and Restraint

- Explain the importance of proper handling and demonstrate appropriate handling techniques (10.7.1-10.7.2).
- Compare various methods of restraining animals and give advantages and disadvantages of each (10.7.3).
- Discuss the following issues related to prolonged restraint, if applicable to the audience:
 - Legal requirements and institutional policies (10.7.4.1).
 - Selection of method, conditioning of animals, and prevention or correction of problems (10.7.4.2).

Identification and Records

- Present the legal requirements for identifying animals and recordkeeping (10.8.1).
- Compare methods of identifying individual animals (10.8.2).
- Describe different methods of recordkeeping (10.8.3).

Animal Health

- Provide normal physiologic and biochemical parameters for the given species (10.9.1).

- Discuss the importance of health surveillance and the role of the research team (10.9.2).
- Describe gross, physiologic, and behavioral signs of distress and disease (10.9.3).
- List common naturally occurring and experimentally induced diseases (10.9.4-10.9.5).
- Discuss procedures for emergency or special care (10.9.6).

Safety and Health Considerations (Zoonoses)

- Discuss naturally occurring and experimentally induced zoonotic diseases, including signs and symptoms in animals and in humans (10.10.1-10.10.2).
- Demonstrate the use of protective clothing and equipment and appropriate techniques for handling high-risk animals (10.10.3).
- Discuss the importance of and mechanisms for reporting incidents.

Specific Techniques

- Describe in detail acceptable methods for performing common procedures such as measurement of vital signs, injections, specimen collection, and blood withdrawal, including type and care of instruments.
- Describe signs of accuracy and of error associated with each procedure and specify what would be done in case of error.
- Present humane and safety considerations associated with such procedures as restraint for the animal or protective clothing for the handler, need for anesthetics and/or analgesics, acceptable frequencies or amounts, signs of distress associated with the procedures, and remedies.

Euthanasia

- Present legal and ethical indications for euthanasia (8.2-8.3).
- Present chemical and physical options, indicating preferred methods and unacceptable methods (8.5-8.7).
- Discuss the emotional effects of euthanasia on personnel (8.4).
- Describe in detail your institution's procedure for carcass disposal, with emphasis on potential hazards to people handling carcasses (8.8).

Skill Building

Allow sufficient time for every participant to:

- Demonstrate ability to handle and restrain an animal.
- Demonstrate ability to determine an animal's sex.
- Take vital signs and assess health.

- Prepare a syringe for use (e.g., add a needle of appropriate gauge for the species and material to be injected).
- Locate structures or landmarks used to guide intraperitoneal, intramuscular, and intravenous injections.
- Prepare equipment and locate structures associated with blood withdrawal.
- Select a pharmacologic method of euthanasia and calculate the required dose.
- Perform specific procedures that will be used in the participant's research.
- Demonstrate the appropriate handling technique for sterile instruments and equipment.
- Demonstrate use of protective clothing, as applicable to the participant's needs.

3

Pain-Management Module

INTRODUCTION

This module builds on information presented in the core and species-specific modules. It is intended as an in-depth study for scientists whose protocols involve surgery or other procedures that are associated with pain or distress. As stated in the species-specific module, demonstrations and visual aids can be helpful in introducing a laboratory exercise; however, these should not be substituted for the hands-on experience needed by the participants to develop their skills.

The recommended content of each topic below is cross-referenced to the expanded outlines contained in Part III, as explained in the core module. This module draws on the material in Chapters 5 (Pain and Distress), 6 (Anesthetics, Analgesics, Tranquilizers, and Neuromuscular Blocking Agents), and 8 (Euthanasia).

OUTLINE FOR THE PAIN-MANAGEMENT MODULE

Definitions, Mechanisms, and Assessment

- Review definitions of discomfort, stress, distress, and pain, and discuss categories of pain (5.1-5.2).
- Explain mechanisms by which pain is perceived and present signs that are used to assess whether an animal is in pain (5.3-5.4).
- Review sources of stress and the value of adaptation to the animal (5.5.1).

- Review sources of distress and signs of maladaptive behavior (5.5.2-5.6).

Legal and Ethical Obligations

- Present in detail ethical and legal obligations for management of pain (5.7-5.8).
- Review the function of the attending veterinarian (5.9, 6.8).

Alleviation of Pain or Distress

- Present nonpharmacologic interventions (5.9.3).
- Differentiate between functions of anesthetics, tranquilizers and sedatives, analgesics, and neuromuscular blocking agents (paralytics) (6.1-6.4).
- Provide examples of one or more pharmacologic agents used for tranquilization, muscle relaxation, and immobilization (6.2-6.4).
- Provide guidelines for selecting and using each of these agents (6.2-6.4).
- List and discuss factors that modify responses of these agents (6.5).
- Review safety precautions and recordkeeping requirements (6.6-6.7).

Anesthesia

- Provide examples of agents commonly used for general anesthesia and for pretreating the patient (6.1.3-6.1.4).
- Present in detail dosage principles (6.1.5).
- Describe the stages of anesthesia and how to assess the plane of anesthesia (6.1.6-6.1.7).
- Discuss signs of overdose and recommended actions in such cases (6.1.8-6.1.9).

Euthanasia

- Review the definition of euthanasia (8.1).
- Present legal requirements and institutional policies in detail (8.2).
- Discuss ethical and humane considerations in performing euthanasia (8.3).
- Discuss the effects that euthanasia can have on personnel, and describe ways to cope with euthanasia-associated stress (8.4).
- Present the criteria for selecting a method of euthanasia (8.5).
- Review acceptable pharmacologic methods of euthanasia and list drugs that should never be used alone for euthanasia (8.6).
- Review acceptable physical methods of euthanasia (8.7).
- Discuss appropriate methods for disposing of carcasses (8.8).

Skill Building

Every participant should have the opportunity to:

- Select appropriate pain-relieving agents for a specific animal in a specific case.
- Calculate and prepare the correct dose.
- Simulate administration.
- Simulate monitoring of effectiveness.

4

Surgery Module

INTRODUCTION

This module builds on information presented in the core, species-specific, and pain-management modules. It is intended as an in-depth study for scientists whose protocols involve the performance of surgical procedures. This module should be species- and procedure-specific insofar as possible. The didactic portions can be covered with directed independent study, and portions of the application can be taught through case problems and simulation. Hands-on experience, however, is needed for skill-building.

The recommended content of each topic below is cross-referenced to the expanded outlines contained in Part III, as explained in the core module. This module draws primarily on the material in Chapter 7 (Survival Surgery and Postsurgical Care), with additional material taken from Chapter 8 (Euthanasia).

OUTLINE FOR THE SURGERY MODULE

Definitions

- Define terms necessary for understanding legal requirements for performing surgery on animals (7.1).

Legal Requirements for Survival Surgery

- Cite the legal requirement for training of personnel performing surgery (7.2.1).

- Discuss the legal requirement for administration of appropriate pain-relieving agents, conditions under which withholding of such agents is acceptable, and legal and institutional requirements for justification for withholding such agents (7.2.2).
- Discuss legal and institutional requirements for pre- and postsurgical care (7.2.3).
- Discuss approved areas for performing surgery and the surgical facilities available at your institution (7.2.4).
- Discuss legal limitations for performing multiple major survival surgeries (7.2.5).

Aseptic Technique

- Demonstrate preparation of an animal for aseptic surgery (7.3.1).
- Demonstrate the preparations of a surgical team for aseptic surgery, including scrubbing, gloving, and gowning (7.3.2).
- Describe preparation of the surgical instruments (7.3.3).

Selection and Administration of Anesthetic

- Review and discuss the types of anesthetics available (6.1.3) and considerations in selecting an anesthetic agent.
- Review the procedure for inducing anesthesia (6.1.4-6.1.6).
- Review the stages of anesthesia and criteria for assessing depth of anesthesia (6.1.7-6.1.8).
- Review the causes of and procedures for dealing with an anesthetic overdose (6.1.9-6.1.10, 7.5.4).

Surgical Complications

- Discuss monitoring and control of body temperature and hydration during surgery (7.5.1-7.5.2).
- Discuss prevention of excess bleeding and how to control hemorrhage if it occurs (7.5.3).

Surgical Techniques

- Review pertinent anatomy relevant to common procedures.
- Introduce surgical instruments and equipment appropriate to given procedures.
- Discuss important considerations in suturing (7.6).

Postsurgical Care

- Describe in detail the care of animals following surgery (7.7).
- List equipment items that are useful during surgery and in providing postsurgical care (7.8).

Medical Records

- Discuss the importance and contents of the surgical records (7.9).

Terminal Surgeries

- Review euthanasia options and selected methods (8.5-8.7).
- Review carcass disposal (8.8).

Skill Building

- Present case problems requiring participants to apply the above principles and procedures to normal situations and potential crises.
- Provide opportunities to observe and participate in surgical procedures pertinent to need.
- Provide opportunities for participants to gain experience in postsurgical care and monitoring.

III

CONTENT OUTLINES

Introduction

This section of the guide contains detailed content outlines of the subjects covered in the recommended modules (Part II). The material in the modules is cross-referenced to appropriate subtopics in this section. The number preceding the decimal point indicates the chapter, and the number(s) following the decimal point indicates the place within the chapter that the information appears. Thus, 1.1 indicates the first entry in chapter 1 of part III, and 1.2.1 indicates the first subentry under the second entry in chapter 1.

Content experts asked to deliver information or teach skills should be provided with both the module outline and the corresponding outlines in this section to determine the intended depth of presentation. These outlines can also be used to select alternative instructional materials (e.g., audiovisual, computer-aided, and independent-study). Some sections can also be used as handouts. Permission for limited reproduction of portions of this book for educational purposes, but not for sale, may be granted on receipt of a written request to the National Academy Press, 2101 Constitution Avenue, Washington, DC 20418.

1

Laws, Regulations, and Policies That Impact on the Care and Use of Animals

1.1 Federal Regulations and Policies Affecting the Care and Use of Animals in Research, Testing, and Education¹

1.1.1 Animal Welfare Regulations (AWRs)

1.1.1.1 Citation: Code of Federal Regulations, Title 9 (Animals and Animal Products), Subchapter A (Animal Welfare), Parts 1-4 (9 CFR 1-4)

1.1.1.2 Law implemented: U.S. Code, Title 7, Sections 2131 et seq. (7 USC 2131 et seq.), popularly called the Animal Welfare Act; most recently amended in 1985 by Public Law (PL) 99-198

1.1.1.3 Enforcing Agency: U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Regulatory Enforcement and Animal Care (REAC)

1.1.1.4 Research institutions to which AWRs are applicable: All research facilities that use or intend to use live animals (as defined by the regulations; see 1.1.1.5) in research, testing, and education

1.1.1.5 Code of Federal Regulations, Title 9, Part 1: Definition of Terms

- Amended regulations became effective October 30, 1989
- Includes in the definition of animal any warmblooded animal used or intended for use in research, testing, or education except birds; rats of the genus *Rattus* and mice of the genus *Mus* bred for use in

¹Because regulations change periodically, it is recommended that the current Code of Federal Regulations be consulted before presenting regulatory material.

research; and horses and other farm animals used or intended for use in agricultural research and production

1.1.1.6 Code of Federal Regulations, Title 9, Part 2

- Amended regulations became effective October 30, 1989
- Subparts A, B, and D-I set rules for dealers, exhibitors, and owners of auction sales. Describe requirements for licensing or registration, identification of animals, and recordkeeping; detail responsibilities of the attending veterinarian; and prohibit the purchase, sale, use, or transportation of stolen animals
- Subpart C sets rules for research facilities; requires compliance with standards in Part 3

1.1.1.7 Code of Federal Regulations, Title 9, Part 3

- Establishes minimum standards for animal husbandry, care, treatment, and transportation
- Amended regulations published for guinea pigs, hamsters, and rabbits (APHIS, 1990a)
- Proposed rules published for dogs, cats, and nonhuman primates (APHIS, 1990b)
 - Revise standards for handling, care, treatment, and transportation of dogs, cats, and nonhuman primates
 - Set standards for exercise and socialization for dogs
 - Set standards for environment enhancement to promote psychological well-being of nonhuman primates

1.1.1.8 Penalties

- Animal Welfare Act (7 USC 2143f; 2149)
 - The institution can be fined up to \$2,500 for each violation of the Animal Welfare Act or the AWRs
 - An order can be issued that the institution cease and desist violations of the act or the AWRs
 - REAC can request federal funding agencies to suspend or revoke funding for research facilities that are in violation of the act or the AWRs
 - REAC can temporarily suspend the licenses of dealers, exhibitors, or owners of auction sales in violation of the act or the AWRs
- Code of Federal Regulations, Title 9, Part 4: Rules of Practice
 - Confers authority for adjudicatory proceedings as defined in CFR, Title 7, Subtitle A, Part 1, Subpart H
 - Gives additional authority for suspending licenses

1.1.2 Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (PHS, 1986)

1.1.2.1 Description

- Intended to ensure that PHS grantees and contractors care for and use animals humanely

- Has been in existence since 1971; underwent major revision in 1985 and minor revision in 1986
 - Implements and supplements the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (see Appendix I)
- 1.1.2.2 Law implemented: U.S. Code, Title 42, Section 289d (42 USC 289d); was amended in 1985 to cover the care and use of animals in research by PL 99-158, the Health Research Extension Act
- 1.1.2.3 Oversight by the PHS Office for Protection from Research Risks (OPRR)
- 1.1.2.4 Activities to which policy is applicable: All PHS-conducted or supported activities involving the use of animals; an animal is defined as "any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes"
- 1.1.2.5 Requirements
- Compliance with the AWRs and the *Guide for the Care and Use of Laboratory Animals*, which was revised most recently in 1985 (NRC, 1985)
 - A written statement of Assurance, including
 - A description of the animal care and use program
 - The qualifications, authority, and responsibility of the program's veterinarian(s)
 - A list of members of the institutional animal care and use committee and procedures these members will follow to fulfill the requirements of PHS policy
 - A summary description of the institution's educational or training programs in humane animal care and use
 - An assurance that the institution is accredited by the American Association for Accreditation of Laboratory Animal Care or has been evaluated by the institution
- 1.1.2.6 Penalty for noncompliance: Revocation of Assurance and loss of PHS support for entire institution
- 1.1.3 Good Laboratory Practice (GLP) standards
- 1.1.3.1 Prescribes good laboratory practice in several sections of the Code of Federal Regulations
- 40 CFR 792 concerns studies on health effects, environmental effects, and chemical fate testing of substances regulated by the Environmental Protection Agency pursuant to 15 USC 2603 et seq. (Toxic Substances Control Act)
 - 40 CFR 160 concerns studies that support or are intended to support applications for research or marketing permits for pesticides regulated by the Environmental Protection Agency pursuant to 7 USC

136a, 136c, 136f, 1136q, 136v(c) (Federal Insecticide, Fungicide, and Rodenticide Act) and 21 USC 346a, 348 (Federal Food, Drug, and Cosmetic Act)

- 21 CFR 58 concerns studies that support or are intended to support applications for research or marketing permits regulated by the Food and Drug Administration pursuant to 21 USC 406, 408-409, 502-503, 505-507, 510, 512-516, 518-520, 706, 801 (Federal Food, Drug, and Cosmetic Act) and 42 USC 351, 354-360F (Public Health Service Act)

1.1.3.2 Main concern is with reliability of research results

1.1.3.3 Subpart C of each of the GLPs

- Requires separate rooms or areas for separation of species, isolation of individual projects, quarantine, and routine or specialized housing
- Requires, as appropriate, separate rooms or areas for diagnosis, treatment, and control of diseases
- Requires, as needed, storage areas for feed, bedding, supplies, and equipment

1.1.3.4 Subpart E of each of the GLPs

- Requires written standard operating procedures for housing, feeding, handling, and care of animals
- Requires appropriate identification of animals
 - 21 CFR 58.90, was amended effective May 22, 1989
 - Amendment prohibits toe clipping as a means of identification
- Requires extensive recordkeeping on the environment of the animal rooms

1.2 Selected Requirements of AWRs and PHS Policy

1.2.1 Institutional animal care and use committee (IACUC)

1.2.1.1 Membership

- Must be appointed by institution's chief executive officer
- Number of members: Chairman and at least two additional members (9 CFR 2.31); Chairman and at least four additional members (PHS, 1986)
- At least one member must be a doctor of veterinary medicine with training or experience in laboratory animal science and medicine and with direct or delegated program responsibility for activities involving animals (9 CFR 2.31; PHS, 1986)
- At least one member must not be affiliated with the facility other than as a committee member and must not be a member of the immediate family of anyone affiliated with the institution (9 CFR 2.31; PHS, 1986)
- At least one member must be a practicing scientist with experience in research involving animals (PHS, 1986)
- At least one member must be a nonscientist (PHS, 1986)

- 1.2.1.2 Functions (see also content outline section 4.2)
 - Reviews semiannually institutional animal facilities and the institutional program for humane animal care and use and reports on these reviews to the institutional official
 - Reviews and approves protocols and modifications to protocols
 - Reviews concerns about care and use of animals
 - Suspends activities found no longer to be in compliance with the AWRs and PHS policy
 - Makes recommendations to the responsible institutional official concerning the animal care and use program, animal facilities, or personnel training
- 1.2.2 Training and Instruction
 - 1.2.2.1 Must be made available to all personnel involved in the care, treatment, and use of species covered by the AWRs and PHS policy
 - 1.2.2.2 Must include at least the following areas
 - Humane methods of animal maintenance and experimentation
 - Methods that limit the use of animals or minimize distress
 - Proper use of anesthetics, analgesics, and tranquilizers for any species used by the facility
 - Methods for reporting deficiencies in care and treatment
 - Utilization of services, such as the National Agricultural Library, that provide information that could prevent unintended or unnecessary duplication of animal research and details about appropriate methods of animal care and use, alternatives to the use of live animals in research, and the intent and requirements of the Animal Welfare Act
- 1.2.3 Records that facilities must keep
 - 1.2.3.1 Records of the IACUC
 - Minutes of meetings
 - Records of applications
 - Proposed significant changes in animal care and use and whether approval was given or withheld
 - Semiannual reports
 - 1.2.3.2 Records on the description, identification, purchase, sale, transportation, and previous ownership of live dogs and cats (AWRs)
 - 1.2.3.3 Records of accrediting body determinations (PHS policy)
- 1.2.4 Required reports
 - 1.2.4.1 AWRs (9 CFR 2.31, 2.36)
 - Requires annual report to REAC made by the facility and certified by the responsible institutional official or the chief executive officer
 - Must contain assurance that professionally acceptable standards were followed in care, treatment, and use; that principal investigators have considered alternatives to painful procedures; and that the facility is adhering to the standards and regulations

and has IACUC approval for all exceptions

- Must state the location of all facilities where animals, as defined by the AWRs, were housed or used
- Must give the numbers and common names of animals, as defined by the AWRs, used in nonpainful or nondistressing procedures, painful or distressing procedures in which appropriate pain-relieving or tranquilizing drugs were given, and painful or distressing procedures in which pain-relieving or tranquilizing drugs were withheld because they would have interfered with experimental results
- Must give the numbers and common names of animals, as defined by the AWRs, bred for use in research, testing, and education but not yet used for such purposes
- Requires prompt notification, with a full explanation, of any suspended activity

1.2.4.2 PHS policy (PHS, 1986)

- Requires annual report to OPRR by the IACUC through the institutional official
 - Must note significant changes in the institution's programs, facilities, or animal care and use program
 - Must list changes in IACUC membership
 - Must provide dates of semiannual IACUC evaluations
- Requires prompt notification with a full explanation of
 - Any serious or continuing noncompliance with PHS policy or the *Guide for the Care and Use of Laboratory Animals*
 - Any suspension of activity by the IACUC

1.3 State and Local Regulations Affecting the Care and Use of Animals in Research, Testing, and Education (if applicable)

1.4 Institutional Policies Affecting the Care and Use of Animals in Research, Testing, and Education

1.4.1 Policies that affect research protocols

1.4.2 Policy on dealing with alleged misconduct

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2

Ethical and Scientific Issues

2.1 Definitions

2.1.1 Ethics: A discipline within philosophy concerned with the examination and establishment of criteria for making judgments concerning value (good and bad) and judgments concerning responsibility and duty (right and wrong)

2.1.2 Applied ethics: Ethical reflection, as defined above, applied to a specific area of concern, e.g., the use of laboratory animals

2.2 Conceptual Framework for Ethical Decisions (Robb, 1989)

2.2.1 A framework provides a method or formal structure for making decisions

2.2.2 Utilitarian or teleological ethical approach to decision making

2.2.2.1 Involves risk/benefit analysis; the best action is determined by the effects of the action in a particular circumstance or on the effects on all concerned (the social utility of the action)

2.2.2.2 Can be used by both animal-rights and animal-use advocates

2.2.2.3 Is too often based on short-term rather than long-term effects

2.2.3 Deontological ethical approach to decision making

2.2.3.1 Determines an action by comparison with a highest duty (e.g., respect for dignity, beneficence, justice) or with universal moral obligations derived from cultural or religious principles

2.2.3.2 Is used primarily by animal-rights advocates

2.2.3.3 By definition, ignores the short- and long-term consequences of an action; however, in actual experience, moral principles have exceptions

It is important that the person who presents the issues discussed in this chapter emphasizes the need for tolerance of differing points of view.

- 2.3 Arguments Used by Those Advocating the Humane Use of Animals for Human Purposes (Caplan, 1984)
 - 2.3.1 Research with animals has made possible the advancement of knowledge in the medical and veterinary sciences in ways that otherwise would not have been possible (NRC, 1988)
 - 2.3.1.1 Benefits of basic research
 - 2.3.1.2 Benefits to health and welfare of humans and animals
 - 2.3.2 Society accepts the idea of a hierarchy of species in its attitude toward other animal species (NRC, 1988, p. 16)
 - 2.3.3 Humankind has the moral responsibility to enhance the well-being of other humans and also the moral duty to use wisely and prudently all resources that nature provides, including the use of animals for good purposes
- 2.4 Arguments Used by Animal-Rights Advocates (Singer, 1975; Regan, 1983)
 - 2.4.1 Animals are intelligent and sentient beings, with feelings not too unlike our own
 - 2.4.2 Animals have inherent value and have a right to fulfill their destiny as independent beings
 - 2.4.3 As independent beings, they are "subjects-of-a-life," that is, they have desires and intentions that should be respected
 - 2.4.4 Therefore, humankind has no right to exploit them for human purposes because this violates their integrity as separate species
- 2.5 The Role of Laws, Regulations, and Policies
 - 2.5.1 Function to prescribe common standards that prevent the abuse of humane standards for the care of animals
 - 2.5.2 Recent policies and guidelines have refined earlier standards and have had a salutary effect on the well-being of laboratory animals
- 2.6 Suggested Ethical Principles (See U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training; Appendix I)
 - 2.6.1 Design procedures relevant to the improvement of health, advancement of knowledge, or good of society (Principle II)
 - 2.6.2 Use appropriate models and consider alternatives (Principle III)
 - 2.6.3 Avoid or minimize pain and distress (Principle IV)
 - 2.6.4 When painful procedures are necessary, use appropriate sedation, analgesia, or anesthesia (Principle V)
 - 2.6.5 Humanely kill animals that would suffer severe or chronic pain (Principle VI)
 - 2.6.6 If an exception to these principles is necessary, it should be assessed and approved by a review group such as the institutional animal care and use committee (Principle IX)

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3

Alternatives

3.1 Definitions

3.1.1 Alternatives (Russell and Burch, 1959)

3.1.1.1 Replacement: Substitution of insentient material for animals or substitution of a lower species, which might be less sensitive to pain and distress, for a higher species

3.1.1.2 Reduction: Reduction in the numbers of animals used to obtain information of a certain amount and precision

3.1.1.3 Refinement: Decrease in the incidence or severity of pain and distress in those animals that are used

3.1.2 Biomedical model: A surrogate system, either animate or inanimate, that mimics or is predictive about a biologic process or condition of interest

3.2 Rationale for Considering Alternatives

3.2.1 Regulatory

3.2.1.1 AWRs (9 CFR 2)

- Principal investigators must consider alternatives to any procedure likely to produce pain or distress
- Assurance that alternatives **have been** considered must be presented in the institution's annual report and when the institution is inspected by the USDA
- Training must be provided by the institution on research or testing methods that minimize or eliminate the use of animals or limit their pain or distress
- The National Agricultural Library, in cooperation with the National Library of Medicine, must provide information that could prevent

- unintended duplication of experiments and that could reduce or replace the use of animals
- 3.2.1.2 PHS policy: Institutions must give assurances satisfactory to the director of NIH that they are making available to scientists, animal technicians, and other personnel instruction or training on availability and use of research or testing methods that limit the use of animals or limit pain and distress (PHS, 1986)
- 3.2.1.3 Institutional policy
- Animal care and use protocol form requirements
 - Review and approval of protocols by the institutional animal care and use committee
- 3.2.2 Ethical
- 3.2.2.1 Do the potential results of the project justify its likely effects on the animal? (Tannenbaum, 1989)
- 3.2.2.2 Is the species endangered or threatened?
- 3.2.3 Humane (OTA, 1986)
- 3.2.3.1 Can procedures be modified to prevent or minimize pain and distress?
- 3.2.3.2 Can analgesics, anesthetics, tranquilizers, or sedatives be used to provide relief from pain and distress?
- 3.2.3.3 Can a less sensitive species be used?
- 3.2.4 Economic
- 3.2.4.1 What are the costs to purchase, house, and care for the animals?
- 3.2.4.2 What are the costs for equipment and supplies for a nonanimal model?
- 3.2.4.3 What is the cost for a noninvasive technique such as ultrasound or magnetic resonance imaging?
- 3.2.4.4 Have nonanimal alternatives been used to screen compounds for efficacy, thus reducing the number of compounds that require testing in animals?
- 3.2.5 Scientific
- 3.2.5.1 Does the model reliably and accurately reproduce the process or characteristic being studied?
- 3.2.5.2 Is the model readily available to other researchers?
- 3.2.5.3 Is the model well characterized in the literature?
- 3.3 Nonanimal Research Methods and Models
- 3.3.1 Literature Search
- 3.3.1.1 Can be used to avoid unnecessary duplication of research
- 3.3.1.2 Can provide a scientific basis for choice of model
- 3.3.2 Epidemiological Research: Can be used to understand the frequency, distribution, and cause of disease, both infectious and noninfectious, in a given population
- 3.3.3 Human Subject Research: If morally and legally acceptable, safe, noninvasive methods to test human subjects can replace the use of animals
- 3.3.4 Cell, tissue, and organ culture systems: Systems derived from humans or

animals and then maintained and propagated replace the need to experiment on living animals or reduce the number of animals used

- 3.3.5 Chemical analysis: Radiological binding assays and radioimmunoassays can be substituted for bioassays

- 3.3.6 Microbiological systems

3.3.6.1 Ames mutagenicity/carcinogenicity test, which uses *Salmonella typhimurium*

3.3.6.2 Recombinant DNA studies of gene control using *Escherichia coli*

- 3.3.7 Plants: Yeasts, in particular, have been used extensively to study basic molecular mechanisms of interest to cellular and molecular biologists and virologists

- 3.3.8 Mathematical Systems

- 3.3.8.1 Statistical design

- Should be applied to all animal research protocols
- Can lead to increases or decreases in the number of animals required in a protocol
- Includes consideration of factors such as statistical power, randomization, and compounding variables

- 3.3.8.2 Computer modeling and analysis

- Computers can be used to study molecular structure and activity relationships
- Models are based on in vivo data expressed in a mathematical equation where parameters can be manipulated to simulate a biological effect
- In vivo systems are required to validate conclusions

- 3.4 Factors Influencing Model Selection

- 3.4.1 Scientific considerations (Animal Alternatives Study Task Force, 1988).

3.4.1.1 Relevancy: Models must have one or more features that resemble the original system

3.4.1.2 Reliability: Models must allow investigators to obtain consistent, reproducible results

3.4.1.3 Simplicity: Simpler models usually provide fewer variables than a whole human or animal and reduce the complexity that can obscure understanding of a specific process

3.4.1.4 Accessibility: Models must be readily available to the research community and permit manipulation using contemporary technology

- 3.4.2 Ethical considerations

3.4.2.1 Safety of research personnel and human subjects

3.4.2.2 Conservation of species

3.4.2.3 Humane care and use of animals

- 3.4.3 Economic considerations

3.4.3.1 Purchase of animals

3.4.3.2 Animal maintenance (food, caging, labor)

- 3.4.3.3 Supplies, equipment, facilities, and labor for the conduct of animal research
- 3.4.3.4 Time required to perform studies
- 3.5 Utilization of Services
 - 3.5.1 Extramural
 - 3.5.1.1 National Agricultural Library (see Appendix II)
 - 3.5.1.2 Centers for alternatives
 - Johns Hopkins Center for Alternatives to Animal Testing (see Part IV, section 1)
 - Rockefeller University Laboratory for In Vitro Toxicologic Assay Development
 - Fund for the Replacement of Animals in Medical Experiments (FRAME)
 - 3.5.1.3 Publications on alternatives (see Part IV, section 2)
 - 3.5.2 Intramural
 - 3.5.2.1 Laboratory animal resources staff
 - 3.5.2.2 Library

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4

Responsibilities of the Institution, the Animal Care and Use Committee, and the Research and Veterinary Staffs

- 4.1 Responsibilities of the Institution
 - 4.1.1 Establishes lines of authority and responsibility
 - 4.1.1.1 Chief executive officer
 - 4.1.1.2 Institutional official, if different from the chief executive officer (see 9 CFR 1.1; PHS, 1986, part III)
 - 4.1.1.3 Animal resource director, if different from the attending veterinarian
 - 4.1.1.4 Attending veterinarian (see 9 CFR 1.1, 2.33)
 - 4.1.1.5 Facility manager: Clarify reporting relationship to institutional official and/or animal resource director
 - 4.1.1.6 Principal investigator
 - 4.1.1.7 Research staff
 - 4.1.1.8 Others, as appropriate to the institution
 - 4.1.2 Establishes and disseminates institutional policy
 - 4.1.2.1 Policy on care and use of animals: Discuss the institution's commitment to
 - An environment conducive to high-quality research, humane treatment of animals, and safety of personnel
 - Compliance with federal, state, and local laws, regulations, and policies
 - 4.1.2.2 Policy for dealing with alleged misconduct
 - 4.1.3 Provides appropriate facilities for animal housing and care
 - 4.1.4 Guarantees sufficient sources of resources to support key personnel and facilities
 - 4.1.5 Appoints the members of the institutional animal care and use committee (see also 1.2.1)

- 4.1.6 Ensures that all scientists, research technicians, animal care technicians, and other personnel involved in the care and use of animals are qualified to perform their duties (see 9 CFR 2.32)
 - 4.1.6.1 Provides training in the following areas:
 - Humane methods of animal care and use
 - The concept, availability, and use of research or testing methods that reduce the use of animals or minimize pain and distress
 - Proper use of anesthetics, analgesics, and tranquilizers
 - Mechanisms by which deficiencies in animal care and treatment should be reported
 - Use of information services and resources
 - 4.1.6.2 Periodically reviews qualifications of personnel
- 4.1.7 Endeavors to build public confidence in animal research
- 4.2 Responsibilities of the Institutional Animal Care and Use Committee (IACUC)
 - 4.2.1 Reviews and approves activities in which animals will be used
 - 4.2.1.1 Ensures that experiments are justifiable on a scientific basis
 - 4.2.1.2 Ensures that new activities and proposed significant changes in ongoing activities are in compliance with federal regulations and policies (see 9 CFR 2.31; PHS, 1986, part IV-C)
 - Procedures must comply with the requirement to avoid or minimize pain, discomfort, and distress
 - Principal investigators must have considered alternatives to procedures that could cause more than momentary or slight pain or distress
 - Principal investigators must provide written assurance that the activities do not unnecessarily duplicate previous experiments
 - Procedures that will cause more than momentary or slight pain and distress:
 - Must be performed with appropriate sedatives, analgesics, or anesthetics unless withholding such agents is justified scientifically
 - Must involve consultation with the attending veterinarian
 - Must not include the use of paralytics without anesthesia
 - Animals that will experience severe or chronic pain or distress that cannot be relieved must be painlessly killed at the end of the procedure or, if it will not interfere with research results, during the procedure
 - Living conditions must be appropriate for the species of animal and contribute to the health and comfort of the animals
 - Sick animals must receive appropriate medical care provided by a qualified veterinarian
 - Personnel conducting procedures on animals must be appropriately qualified and trained in these procedures
 - All survival surgery must be performed using aseptic procedures, and

- appropriate pre- and postoperative care must be provided
- Major surgical procedures on all animals except rodents must be performed in facilities intended for that purpose
- Animals must not be used in more than one major surgical procedure from which they are allowed to recover unless such use is
 - Justified for scientific reasons in writing
 - Required to protect the health or well-being of the animal as determined by the attending veterinarian
 - A special circumstance approved by the administrator of the Animal and Plant Health Inspection Service, U.S. Department of Agriculture
- Methods of euthanasia must be in compliance with federal regulations and policies
- 4.2.1.3 Conducts continuing reviews of ongoing activities at appropriate intervals, but not less than annually
- 4.2.1.4 Suspends activities not conducted in accordance with IACUC-approved protocols
- 4.2.2 Evaluates the institutional program for humane care and use of animals and inspects all animal facilities at least once every 6 months (see 9 CFR 2.31; PHS, 1986, part IV-B)
 - 4.2.2.1 Prepares a report on the findings of each evaluation and inspection, including all minority opinions, and submits its report to the institutional official
 - Points out areas in which the institution does not adhere to AWRs and distinguishes significant from minor deficiencies
 - Includes a plan and schedule for correcting the deficiencies
 - 4.2.2.2 Reviews and, if warranted, investigates allegations of noncompliance
 - 4.2.2.3 Makes recommendations on the animal program, animal facilities, and personnel training to the institutional official
- 4.3 Responsibilities of the Investigator (The term investigator is used broadly to designate those people responsible for the scientific aspects of projects that use animals in research, testing, or teaching)
 - 4.3.1 Designs experiments
 - 4.3.1.1 Selects the appropriate species, model, animal quality, and source; consults with a statistician to determine the minimum number of animals required for valid data analysis
 - 4.3.1.2 Considers previous work done in the area of study, using resources such as databases of the National Agricultural Library and National Library of Medicine
 - Considers possible alternatives to living animals as subjects
 - Ensures that studies will not unnecessarily duplicate previous experiments
 - 4.3.1.3 Establishes procedures and environments that minimize internal and

- external influences on experimental animals
- 4.3.1.4 Avoids, prevents, or minimizes animal discomfort, distress, and pain, consistent with sound scientific practice
- 4.3.1.5 Uses appropriate endpoints for studies and acceptable procedures for euthanasia
- 4.3.1.6 Conducts all research in accordance with protocols approved by the IACUC
- 4.3.1.7 Procures all laboratory animals in accordance with federal and institutional regulations and policies
- 4.3.1.8 Maintains adequate records
- 4.3.2 Ensures staff qualifications and training
 - 4.3.2.1 Recruits personnel qualified by background and temperament to work with animals
 - 4.3.2.2 Orients personnel to the facility and the scientific study
 - 4.3.2.3 Requires that staff members demonstrate skill with the techniques and procedures involved; provides training as needed
 - 4.3.2.4 Ensures that staff members are able to recognize signs of disease and distress in animals and know to whom to report any such signs
 - 4.3.2.5 Provides or identifies continuing education programs for staff and encourages participation in such programs
- 4.3.3 Provides for health and safety of personnel
 - 4.3.3.1 Ensures that staff have had instruction and training about zoonotic diseases, allergies to animals, occupational health programs, and disease prevention
 - 4.3.3.2 Ensures that staff have received detailed instructions on proper procedures for using hazardous substances, including the requirement for protective clothing appropriate for the species of animal and the protocol
- 4.3.4 Makes provisions for dealing with job-related stress (see also 8.4)
 - 4.3.4.1 Identifies activities and procedures that might be stressful to personnel, including euthanasia, long-term studies, and studies using animals generally regarded as pets
 - 4.3.4.2 Provides opportunities for stress-reduction training for all employees involved in high-stress activities
 - 4.3.4.3 Gives particular attention to reducing stress in inexperienced, naive, and highly emotional employees before and during studies
- 4.3.5 Maintains a scholarly, sensitive, and respectful environment and behaves in a professional manner
- 4.3.6 Endeavors to build public confidence in animal research
 - 4.3.6.1 Provides a lay-language description of studies and procedures for the IACUC and for other institutional purposes
 - 4.3.6.2 Might participate in community programs to promote understanding of the need for and role of animals in research, testing, and teaching

- 4.4 Responsibilities of the Attending Veterinarian (see 9 CFR 2.33)
 - 4.4.1 If so designated by the institution, directs the housing, feeding, and nonmedical care of experimental animals
 - 4.4.2 If so appointed by the institution, serves as a voting member of the IACUC
 - 4.4.3 Ensures the provision of adequate veterinary care for experimental animals
 - 4.4.3.1 Establishes appropriate programs to prevent, control, diagnose, and treat diseases and injuries
 - 4.4.3.2 Ensures that appropriate pre- and postprocedural care will be provided in accordance with established veterinary medical and nursing procedures
 - 4.4.3.3 Ensures that emergency, weekend, and holiday care will be provided
 - 4.4.3.4 Ensures that animals will be observed daily to assess their health and well-being and to ensure that problems are reported quickly
 - 4.4.4 Provides guidance to principal investigators and other personnel regarding animal handling, immobilization, anesthesia, analgesia, tranquilization, and euthanasia

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5

Pain and Distress

5.1 Definitions

- 5.1.1 Comfort: A state of physiologic and behavioral homeostasis in which the animal has adapted to its environment and shows normal feeding, drinking, and grooming patterns; social interactions; sleep/wake cycles; and reproductive activity (NRC, in press)
- 5.1.2 Discomfort: A minimal change in an animal's adaptive level or state of homeostasis as a result of changes in its environment or because of biologic, physical, social, or psychologic alterations (NRC, in press)
- 5.1.3 Stress: The effect produced by external (e.g., physical and environmental) events or internal (e.g., physiologic or psychologic) factors that are referred to as stressors and that induce an alteration in an animal's homeostatic or adaptive state (NRC, in press)
- 5.1.4 Distress: An inferred aversive state based on a variety of behavioral, physiologic, and psychologic indices of an animal's inability to adapt to the effect of stressors and the attendant stress (NRC, in press)
- 5.1.5 Pain
 - 5.1.5.1 The sensation (perception) resulting from nerve impulses reaching the cerebral cortex via specific neural pathways (nociceptive pathways) (AVMA, 1986)
 - The term nociceptive is derived from Latin words meaning "hurtful stimulus"
 - Noxious stimuli damage or destroy tissue or have the potential to do so

- Noxious stimuli initiate nerve impulses by acting on a specific set of receptors called nociceptors
- Nociceptors respond to excessive mechanical, thermal, or chemical stimuli
- 5.1.5.2 An unpleasant sensory or emotional experience associated with potential or actual tissue damage (Mersky, 1986)
- 5.2 Categories of Pain (AVMA, 1986)
 - 5.2.1 Sensory-Discriminative: Provides sensory information about the intensity, duration, and location of a stimulus causing pain
 - 5.2.2 Motivational-Affective: Provides affective information about the severity and quality of a stimulus causing pain
- 5.3 Pain Perception
 - 5.3.1 Range: From pain detection threshold through upper limit of pain tolerance
 - 5.3.1.1 Pain detection threshold: That point at which pain is first perceived during noxious stimulation
 - Minimal pain, not associated with stress or distress (Wolff, 1978)
 - Same in animals and in humans (Vierck, 1976; Zimmerman, 1984; Kitchell, 1987)
 - 5.3.1.2 Pain tolerance
 - Limit of tolerance to noxious stimuli
 - Varies between individuals and between species
 - 5.3.2 Duration
 - 5.3.2.1 Acute pain
 - Short duration
 - Occurs after injury or early in illness
 - Plays protective role, warning the body about injury
 - 5.3.2.2 Chronic pain
 - Longer duration than acute pain
 - Does not serve protective role
 - 5.3.3 Pain is perceived only if the cerebral cortex and subcortical structures are functional; it is not perceived if these structures are rendered nonfunctional (e.g., by hypoxia, drugs, electrical shock, concussion, surgical intervention)
 - 5.3.4 Pain can be perceived even though noxious stimuli do not elicit body movements (e.g., if a muscle-paralyzing drug such as succinylcholine is administered)
- 5.4 Assessment of Pain (AVMA, 1986)
 - 5.4.1 Must be based primarily on observations of abnormal behavioral and physiologic responses that demonstrate anxiety and fear (e.g., distress vocalization, struggling, stumbling, escape activity, defensive aggression or freezing, muscular tremors, pupillary dilation, salivation, reflex urination and defecation, panting and sweating, tachycardia)
 - 5.4.2 Stimuli that evoke a pain response in a conscious animal might elicit only reflex responses in an unconscious animal; therefore, nonpurposeful movements are not reliable indicators of pain perception

5.5 Stress (NRC, in press)

5.5.1 Stress as an adaptive process

5.5.1.1 Stress is not always abnormal or harmful to well-being

- May result from environmental alterations that are not harmful and may initiate responses leading to beneficial effects
- Stressors are common in the natural environment; a captive animal that has not experienced some stress is quite different behaviorally and physiologically from the typical members of its species

5.5.1.2 Response to short-term stress

- Animal attempts to adapt behaviorally and/or physiologically
- Usually no long-term effects
- Introduction of novel stimuli (e.g., exposure to new handling techniques) into the laboratory animal's environment may teach it to adapt more easily to changes that may occasionally occur

5.5.1.3 Acute stress response

- Generally of shorter duration than maladaptive stress (distress) responses
- Causes atypical but not maladaptive behavior under the circumstances (e.g., chairing an unadapted nonhuman primate)
- Important from perspective of both animals and research

5.5.2 Stress as a maladaptive process

5.5.2.1 Stress becomes harmful when an animal cannot adapt to a stressor

5.5.2.2 Stress leading to maladaptive behavior and distress

- Unrelieved pain (e.g., injury, surgery, experimental)
- Anxiety and fear
- Social deprivation
- Boredom
- Inappropriate housing or husbandry practices
- Experimental design

5.6 Distress (NRC, in press)

5.6.1 The relationship between the presence of stress and the process by which an animal proceeds from a state of comfort or discomfort to one of distress poses the same questions that arise whenever one attempts to relate physiologic processes to subjective experience

5.6.2 Response to prolonged stress

5.6.2.1 Maladaptive behaviors: Abnormal feeding and postprandial grooming, inappropriate interaction with cohorts or handlers (e.g., aggression, passivity, withdrawal), inefficient reproduction, stereotypic behavior (?)

- May become permanent part of animal's behavioral repertoire
- Become more maladaptive as the state of distress becomes more extreme or excessive

5.6.2.2 Pathologic conditions (e.g., gastric and intestinal lesions, hypertension, immunosuppression)

5.7 Ethical Obligations

- 5.7.1 Principle of nonmaleficence: Cause no unnecessary pain or distress
- 5.7.2 Principle of beneficence: Be kind whenever possible
- 5.7.3 Procedures selected in designing a study should be based on predictability of outcome
- 5.7.4 To predict outcome, use as comparisons examples with documented characteristics related to the presence or absence of pain and/or distress (Ad Hoc Committee on Animal Research, 1988)

5.8 Legal Obligations (Overseen by the Institutional Animal Care and Use Committee)

- 5.8.1 Scientific procedures must avoid or minimize discomfort, distress, and pain (9 CFR 2.31), consistent with sound research design (PHS, 1986)
- 5.8.2 Principal investigators must have considered alternatives to procedures that might cause more than momentary or slight pain or distress (9 CFR 2.31)
- 5.8.3 Appropriate sedation, analgesia, or anesthesia must be used for procedures that can cause more than momentary or slight pain or distress to the animals, unless withholding such agents is justified for scientific reasons and those reasons are stated in writing (9 CFR 2.31; PHS, 1986)
- 5.8.4 Potentially painful and distressful procedures must be planned in consultation with the attending veterinarian (9 CFR 2.31)
- 5.8.5 Neuromuscular blocking agents (paralytics) must not be used without anesthesia when performing painful or distressful procedures (9 CFR 2.31, NRC, 1985; PHS, 1986)
- 5.8.6 Euthanasia must be performed at the end of a procedure or, if possible, during a procedure in which animals experience severe or chronic pain or distress that cannot be relieved (9 CFR 2.31; PHS, 1986)

5.9 Adequate Veterinary Care

- 5.9.1 Veterinary staff must be able to recognize and advise scientific staff on signs of pain or distress in animals
- 5.9.2 Veterinary staff must be familiar with and advise scientific staff on appropriate interventions for relief of pain or distress
 - 5.9.2.1 Pharmacologic interventions (pain and pain-induced distress)
 - Chemical interventions vary significantly between species, by dose, and by route of administration
 - Analgesics temporarily abolish awareness of pain without loss of consciousness, although their mechanism of action in animals is not yet clearly defined
 - Tranquilizers and sedatives can be used to prevent or diminish distress
 - Anesthetics block perception of pain
 - Neurosurgical lesions block perception of pain
 - 5.9.2.2 Nonpharmacologic interventions (distress not induced by pain)
 - Rearrangements in social groupings may alleviate stressful conditions
 - Addition of bedding material might increase physical comfort

- Gentle handling might decrease distress
- Adaptation to experimental situation before start of study might decrease stress

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6

Anesthetics, Tranquilizers, Analgesics, and Neuromuscular Blocking Agents

6.1 General Anesthetics (Lumb and Jones, 1984)

6.1.1 Definition: Substances that produce, in a controllable manner, a drug-induced absence of perception of all sensation (Marshall and Longnecker, 1990)

6.1.2 Functional Use: To produce unconsciousness, analgesia, and muscle relaxation sufficient to perform procedures painlessly

6.1.3 Classification

6.1.3.1 Injectable: Agents such as the barbiturates (e.g., sodium pentobarbital)

- Effects of these agents cannot be reversed quickly
- Drug must be metabolized, excreted, or counteracted by another drug to terminate anesthetic action

6.1.3.2 Inhalant: Volatile agents (e.g., methoxyflurane, halothane)

- Effects of these agents can be reversed quickly
- Animal's expiration eliminates agent when administration is discontinued

6.1.3.3 Dissociative: Agents that depress the central nervous system (CNS) and produce a state of catalepsy (e.g., ketamine, phencyclidine)

- Have strong analgesic properties in some species
- When used alone, procedures are usually limited to minor surgery
- Most effective when combined with tranquilizers and sedatives (e.g., xylazine, acetylpromazine maleate, diazepam)

The report of the Institute of Laboratory Animal Resources Committee on Pain and Distress in Laboratory Animals entitled *Recognition and Alleviation of Pain and Distress in Laboratory Animals*, which is in press, will provide details on drug actions, drug doses, and species variability.

- Produce seizures and clonic tonic muscle contractions in some species
- 6.1.4 Pretreatment of patient
 - 6.1.4.1 Anticholinergics such as atropine reduce salivation and bradycardia
 - 6.1.4.2 Tranquilizers such as acetylpromazine calm the animal and facilitate restraint
 - 6.1.4.3 Sedatives such as xylazine depress the CNS
- 6.1.5 Dosage principles for general anesthesia
 - 6.1.5.1 Evaluate the physical condition of the animal to ensure the absence of any disease condition that might compromise the animal's health during anesthesia
 - 6.1.5.2 Administer to effect
 - 6.1.5.3 Calculate dose by body weight, taking animal's age into account
 - 6.1.5.4 Allow for variations in response to agent between species and between individuals of the same species because of differences that can occur in absorption and biotransformation
 - 6.1.5.5 Pretreat with tranquilizers or sedatives, when appropriate, to decrease the amount of anesthetic needed
- 6.1.6 General Considerations
 - 6.1.6.1 When possible, a new anesthetic regimen should be tested in a limited number of animals before depending on it for surgical or other painful procedures in a research protocol
 - 6.1.6.2 The health of animal should be considered in selecting an anesthetic
 - 6.1.6.3 The level of CNS depression should be the minimum that is necessary to perform the procedure, compatible with the animal's welfare
 - 6.1.6.4 The effect of anesthesia on the validity of experimental results and the interaction of anesthesia with other drugs in the experimental protocol must be considered
 - 6.1.6.5 Basic equipment to ensure adequate ventilation should be available
 - 6.1.6.6 Body heat must be conserved, especially in small and young animals
 - 6.1.6.7 Whenever possible, a warm, balanced electrolyte solution should be administered by intravenous drip throughout the surgical procedure to help maintain normal hemodynamics
 - 6.1.6.8 The anesthetist is responsible for the animal's welfare until the animal has normal cardiopulmonary function and is able to maintain itself in sternal recumbency
 - 6.1.6.9 Consideration must be given to the safety of personnel in the area where anesthetic gases will be administered and, if necessary, a gas-scavenging system must be provided
- 6.1.7 Stages of general anesthesia
 - 6.1.7.1 Stage I
 - Stage of analgesia or voluntary movement
 - Duration: From onset of administration to loss of consciousness

- 6.1.7.2 Stage II
 - Stage of delirium or involuntary movement
 - Duration: From loss of consciousness to onset of regular pattern of breathing
- 6.1.7.3 Stage III
 - Stage of surgical anesthesia
 - Characterized by unconsciousness; a progressive depression of cardio-pulmonary function; a progressive depression of reflexes, including vomiting and swallowing reflexes; and muscular relaxation
 - Divided into planes 1 through 4, where plane 1 is light, planes 2 and 3 are medium, and plane 4 is deep anesthesia
- 6.1.7.4 Stage IV
 - Characterized by extreme CNS depression
 - Death ensues quickly unless resuscitative steps are taken
- 6.1.8 Evaluation of effects
 - 6.1.8.1 Test reflexes (e.g., pedal and palpebral reflexes) and the tone of the jaw and anal sphincter muscles (reflexes are absent and muscle tone is relaxed during anesthesia)
 - 6.1.8.2 Monitor depth and rate of respiration (increase in depth and decrease in rate signify anesthesia)
 - 6.1.8.3 Monitor heart rate (slowing indicates anesthesia an increase in rate during the procedure often indicates that the depth of anesthesia is not adequate and the animal is feeling pain)
 - 6.1.8.4 Monitor body temperature and maintain at normal levels (temperature falls in anesthesia, especially in small species)
- 6.1.9 Indications of anesthetic overdose
 - 6.1.9.1 Pulse is weak to imperceptible
 - 6.1.9.2 Blood pressure is reduced to shock level
 - 6.1.9.3 Cardiac dysrhythmias may occur
 - 6.1.9.4 Capillary refill time progressively slows to 3 or more seconds
 - 6.1.9.5 Respiration is slow and irregular, becomes diaphragmatic, or may cease
 - 6.1.9.6 Mucous membrane and skin colors may be pale to cyanotic
 - 6.1.9.7 Cardiovascular, CNS, musculoskeletal, gastrointestinal, and ocular reflexes are greatly diminished or cease
- 6.1.10 Intervention for anesthetic overdose
 - 6.1.10.1 Mechanically ventilate with oxygen
 - 6.1.10.2 Administer isotonic fluids intravenously or intraperitoneally
 - 6.1.10.3 Warm animal to increase body temperature
 - 6.1.10.4 Administer antidote, if one exists
- 6.2 Tranquilizers and Sedatives (Gleed, 1987)
 - 6.2.1 Definition
 - 6.2.1.1 Substances that reduce the anxiety and stress that an animal may experience when it is handled

- 6.2.1.2 Distinction between tranquilizers and sedatives is mainly semantic, except that increased doses of tranquilizers tend to produce side effects without loss of consciousness, whereas increased doses of sedatives produce a profound CNS depression resembling anesthesia
- 6.2.2 Functional uses
 - 6.2.2.1 Chemical restraint
 - 6.2.2.2 Preanesthetic medication to reduce amount of anesthetic required
- 6.2.3 Functional characteristics
 - 6.2.3.1 Except for the thiazine derivatives (e.g., xylazine, detomidine), there is no significant analgesic activity
 - 6.2.3.2 Increased stimulation (e.g., noise) usually reverses calming effects
 - 6.2.3.3 When used as preanesthetics:
 - Ample time should be allowed to achieve the maximum effect before inducing anesthesia
 - Recovery from general anesthesia is generally smoother
 - 6.2.3.4 All share the characteristics listed above, but each drug or group of drugs has its own pharmacologic properties and contraindications
- 6.2.4 Classifications of tranquilizers (ataractics or neuroleptics)
 - 6.2.4.1 Phenothiazines (e.g., acetylpromazine)
 - 6.2.4.2 Butyrophenones (e.g., azaperone, droperidol)
 - 6.2.4.3 Benzodiazepines in lower doses (e.g., diazepam, zolazepam)
- 6.2.5 Classifications of sedatives (hypnotics)
 - 6.2.5.1 Barbiturates (e.g., phenobarbital)
 - 6.2.5.2 Benzodiazepines in higher doses (e.g., diazepam, zolazepam)
 - 6.2.5.3 Chloral derivatives (e.g., chloral hydrate)
 - 6.2.5.4 Thiazine derivatives (e.g., xylazine)
- 6.2.6 Tranquilizer and sedative effects
 - 6.2.6.1 Phenothiazines
 - Make animals more tractable
 - Cause hypotension
 - Minimally reduce respiratory rate
 - 6.2.6.2 Butyrophenones
 - Make animals indifferent to their surroundings
 - Decrease motor activity
 - Cause hypotension
 - Slightly increase respiratory rate
 - 6.2.6.3 Benzodiazepines
 - Cause CNS depression
 - Have mild cardiovascular depressant effects at low doses
 - Have little effect on respiration
 - 6.2.6.4 Thiazine derivatives (e.g., xylazine)
 - Produce dose-related CNS depression
 - Have little effect on respiration

- Cause bradycardia, decreased cardiac output, and increased central venous pressure
- 6.2.6.5 Barbituates (e.g., sodium pentobarbital)
 - High doses produce anesthesia
 - At lower doses, sodium pentobarbital can be used as a sedative and premedicant before anesthesia, but a suboptimal (low dose) may cause involuntary excitement in some species
- 6.2.6.6 Chloral derivatives (e.g., chloral hydrate)
 - Is a reliable sedative hypnotic
 - Has poor analgesic properties, even at anesthetic doses
- 6.2.7 Indications for use and monitoring of effects
- 6.2.8 Reversal of tranquilizing and sedative effects
 - 6.2.8.1 No agents available for most tranquilizers and sedatives
 - 6.2.8.2 Yohimbine can be used to reverse xylazine
- 6.3 Analgesics
 - 6.3.1 Definition: Substances that temporarily alleviate pain without causing loss of consciousness
 - 6.3.2 Functional Uses
 - 6.3.2.1 Pain control without the use of anesthetics
 - 6.3.2.2 Preanesthetic to reduce amount of anesthetic required
 - 6.3.2.3 Postoperative pain relief
 - 6.3.3 Classifications
 - 6.3.3.1 Opioids: Term used to designate all endogenous and exogenous substances that bind to a subset of opioid receptors and produce analgesia and mild sedation (e.g., morphine, meperidine, oxymorphone, pentazocine)
 - 6.3.3.2 Opiates: Term no longer used
 - 6.3.3.3 Nonopioids: Drugs such as the alpha-2 agonists that bind at the adrenoceptor sites (e.g., xylazine, detomidine)
 - 6.3.4 Opioids (Short, 1987a)
 - 6.3.4.1 Actions (may vary significantly between species)
 - Major effects on the CNS
 - Effects include analgesia, sedation, respiratory depression, decreased gastrointestinal motility, nausea, vomiting, and alterations of endocrine and autonomic nervous system functions
 - Act as agonists, interacting with binding sites or receptors in the brain and other tissues
 - Actions of some compounds have not been determined for some laboratory animals
 - Dose may vary significantly between species
 - 6.3.4.2 Antagonists: Drugs (e.g., naloxone) that can prevent or promptly reverse some or all of the effects of opioids by competing with them for the same receptor sites

- 6.3.5 Neuroleptanalgesics: Drugs that produce a state of CNS depression and analgesia without the use of barbiturates or volatile anesthetic agents (Short, 1987b)
- 6.3.5.1 Functional use
- Limited applications for minor diagnostic and surgical procedures that require minimal analgesia and immobilization (e.g., radiography, minor skin suturing, placement of peripheral venous catheters)
 - Often require supplementation with additional anesthetics to increase analgesia and muscle relaxation
- 6.3.5.2 Functional characteristics
- Combination of a narcotic (fentanyl) and a tranquilizer (droperidol) such as Innovar-Vet, which produces a state of analgesia and deep sedation without total unconsciousness
 - States of deep sedation and analgesia adequate for surgical intervention have been produced in dogs, rats, and nonhuman primates
 - A peculiar characteristic of this state in the dog and rat, but not in the nonhuman primate, is the capacity to respond to auditory stimuli (e.g., dropping an object, crumpling paper)
 - Pedal reflex is absent
 - Maximum analgesia persists for 30-40 minutes, after which there may be a reaction to cutaneous stimulation even though generalized sedation and some analgesia are still evident
- 6.3.6 Nonsteroidal antiinflammatory drugs (NSAIDs)
- 6.3.6.1 Drugs such as phenylbutazone, acetaminophen, and aspirin can be useful in special cases
- 6.3.6.2 Aspirin
- Most effective for relief of muscular pain
 - Minimal effect for relief of visceral pain
- 6.4 Neuromuscular Blocking Agents (Paralytics or Immobilizing Agents)
- 6.4.1 Definition: Drugs that reduce muscle tone without the loss of consciousness by acting on the neuromuscular junction (e.g., pancuronium) or on spinal synapses (e.g., mephenesin, guaifenesin)
- 6.4.2 Functional Use: Adjuvant in surgical anesthesia to increase muscle relaxation for procedures such as bone fracture repair in heavily muscled animals
- 6.4.3 Effects
- 6.4.3.1 Spinal polysynaptic reflexes are depressed preferentially over monosynaptic reflexes
- 6.4.3.2 Muscle paralysis occurs without loss of consciousness or analgesia; these drugs must never be used without general anesthesia (9 CFR 2.31; NRC, 1985; PHS, 1986)
- 6.4.4 Classification
- 6.4.4.1 Depolarizing agents such as decamethonium and succinylcholine
- 6.4.4.2 Nondepolarizing agents such as tubocurarine USP, gallamine, and pancuronium

- 6.5 Factors Modifying the Effects of Tranquilizers, Analgesics, and Neuromuscular Blocking Agents
 - 6.5.1 Species variation
 - 6.5.2 Age of animals: Very young and old animals may require adjustments in dose
 - 6.5.3 Health status
 - 6.5.3.1 Sick animals may respond differently from healthy animals
 - 6.5.3.2 Pregnant animals may respond differently from nonpregnant animals
 - 6.5.4 Route of drug administration
 - 6.5.5 Depth of anesthesia modifies effects of neuromuscular blocking agents
 - 6.5.6 Others
- 6.6 Safety Precautions
 - 6.6.1 There must be secure storage for drugs with the potential for human abuse
 - 6.6.2* Drugs under the control of the Drug Enforcement Agency must be stored in a locked cabinet in a secure area
- 6.7 Recordkeeping Requirements
 - 6.7.1 A written record is required when barbiturates and other drugs under the control of the Drug Enforcement Agency are used
 - 6.7.2 An inventory list of anesthetics, analgesics, tranquilizers, sedatives, and other drugs should be kept
 - 6.7.3 Individual clinical records should be annotated to reflect the use of the agents described above, showing the date, dose, and any abnormal reactions that occurred
- 6.8 Functions of the Attending Veterinarian in Pain Management
 - 6.8.1 Provides professional advice on the type of agents that are appropriate for use and establishes dose ranges for each
 - 6.8.2 Provides or counsels investigators on appropriate physical facilities and equipment to properly administer general anesthetics
 - 6.8.3 Recommends ways to monitor the physical condition of an animal while it is under treatment
 - 6.8.4 Provides the professional expertise to respond appropriately to medical emergencies if they occur
 - 6.8.5 Monitors procedures to assess degree of pain relief required

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Survival Surgery and Postsurgical Care

7.1 Definitions

- 7.1.1 Aseptic technique: Surgical technique conducted under conditions that prevent exposure of the patient to pathogenic organisms, including wearing of sterile surgical gloves, gowns, caps, and face masks; use of sterile instruments; and aseptic preparation of the surgical field (NRC, 1985, p. 37)
- 7.1.2 Survival surgery: Surgery performed on a live animal under general anesthesia, from which the animal is expected to recover
- 7.1.3 Nonsurvival surgery: The animal is killed at the end of the surgical procedure before recovering from anesthesia
- 7.1.4 Major operative procedure (9 CFR 2.31) or major survival surgery (NRC, 1985, p. 37): Surgical intervention that penetrates a body cavity or could potentially produce a permanent handicap in an animal that is expected to recover
- 7.1.5 Minor surgical procedure: Surgical procedure restricted to the management of minor problems and injuries (e.g., wound suturing, peripheral vessel cannulation)

7.2 Legal Requirements (9 CFR 2.31; PHS, 1986)

- 7.2.1 Surgery must be performed or directly supervised by trained, experienced personnel
- 7.2.2 Procedures that will cause more than momentary or slight pain or distress must be performed with appropriate sedatives, analgesics, or anesthetics, unless withholding such agents is justified for scientific reasons and that justification is provided to the institutional animal care and use committee (IACUC) in writing by the principal investigator
- 7.2.3 Pre- and postsurgical care must be provided in accordance with established veterinary medical and nursing practices

- 7.2.4 Survival surgery
 - 7.2.4.1 AWRs require that aseptic surgical techniques be used on all regulated animals (9 CFR 2.31)
 - 7.2.4.2 PHS policy requires compliance with the *Guide for the Care and Use of Laboratory Animals*, which recommends that survival surgery on rodents be conducted using sterile instruments, surgical gloves, and aseptic procedure (NRC, 1985; PHS, 1986)
 - 7.2.4.3 Major surgical procedures on nonrodents must be conducted only in facilities that are intended for that purpose and are maintained under aseptic conditions (9 CFR 2.31; PHS, 1986)
 - 7.2.4.4 Nonmajor operative procedures, operative procedures conducted at field sites, and all surgical procedures on rodents do not require a dedicated facility but must be performed using aseptic procedures (9 CFR 2.31)
- 7.2.5 Multiple major surgical procedures on one animal may not be performed unless one of the following conditions is met:
 - 7.2.5.1 The procedures are justified for scientific reasons and have been approved by the IACUC; the justification must be stated in writing by the principal investigator
 - 7.2.5.2 The procedures are necessary to protect the health or well-being of the animals, as determined by the attending veterinarian
 - 7.2.5.3 There are special circumstances that have been approved by the administrator of the Animal and Plant Health Inspection Service, U.S. Department of Agriculture, on an individual basis
- 7.3 Preparation for Surgery
 - 7.3.1 Animal
 - 7.3.1.1 Hair should be clipped from the surgical site; special care is necessary when electric clippers are used, because the skin of most laboratory animals is very thin and easily abraded by clipper blades
 - 7.3.1.2 The operative site should be thoroughly cleaned with a skin disinfectant to remove surface bacteria
 - 7.3.1.3 Tape or lightweight strings should be used to secure an animal's limbs and hold the animal in position on the operative table or board
 - 7.3.1.4 The animal should be positioned with the head and neck fully extended to ensure a patent airway, and an endotracheal tube should be inserted when possible
 - 7.3.1.5 Surgical drapes should be used to cover the animal's body to prevent contamination of the operative site; if a drape is used in surgery on rodents and rabbits, the drape must be small enough to permit visualization of the animal's respiratory movements and peripheral perfusion to avoid anesthetic accidents
 - 7.3.2 Surgeon
 - 7.3.2.1 A cap and face mask should be donned first

7.3.2.2 Hands and arms are scrubbed thoroughly with germicidal soap prior to donning sterile gloves and, when appropriate, a surgical gown

7.3.3 Surgical instruments

7.3.3.1 All instruments must be wrapped in packs and sterilized prior to surgery

7.3.3.2 The sterilization date should be written on the outside of each pack when it is prepared

7.3.3.3 Unused, sterilized instruments in packs should be resterilized after a period of time appropriate to the type and thickness of the material in which the instruments are packed and the method of sterilization

7.4 Anesthesia (see section 6.1)

7.5 Surgical Complications

7.5.1 Hypothermia: Abnormally low body temperature caused by inadvertent loss of body heat or purposeful chilling of the animal (Lumb and Jones, 1984)

7.5.1.1 Effects

- Can cause a fall in blood pressure due to decreased cardiac output; however, peripheral resistance increases
- Occasionally causes a severe drop in blood pressure due to depression of the sinoatrial node and bundle of His
- Can cause ventricular fibrillation, most frequently when the temperature of the heart muscle is below 28°C
- In dogs, a fall in body temperature to between 23°C and 15°C can cause a cardiac crisis characterized by cessation of sinus rhythm, intense bradycardia, ventricular extrasystoles, and ventricular fibrillation or standstill
- Prolongs clotting time

7.5.1.2 Occurrence

- Sooner in small rodents and rabbits than in larger animals
 - Small animals have a greater ratio of body surface to body mass than do larger animals
 - Small animals have efficient heat-dissipation surfaces in the ears (rabbits) or in the ears, feet, and tail (rodents)
- When abdominal or thoracic contents are exposed for prolonged periods

7.5.1.3 Prevention—Retaining body heat by using the following:

- Surgical drapes and a pad of insulation placed between the animal's body and the surgery table
- Circulating hot water pads; safer than electric pads because they are less likely to cause tissue damage from localized overheating
- Small, readily sanitizable plastic boards to cover steel table surfaces
- Warm, wet lap sponges to cover exposed organs

7.5.2 Dehydration

7.5.2.1 Can occur when abdominal or thoracic contents are exposed for prolonged periods; therefore, these organs should be covered with

- warm, wet lap sheets or sponges throughout the surgical process
- 7.5.2.2 Can be controlled by administering isotonic electrolyte solutions intravenously to maintain body fluid balance
- 7.5.3 Hemorrhage
 - 7.5.3.1 Causes
 - Improper use of or inadequate hemostatic techniques during surgery (e.g., cautery of small blood vessels or ligatures applied to larger vessels)
 - Intercurrent disease
 - Drugs that prolong bleeding time
 - 7.5.3.2 Prevention: Use of proper surgical techniques
 - 7.5.3.3 Treatment
 - Locate source of bleeding and properly seal open end of vessel(s)
 - If adequate, application of pressure
 - Agents that enhance clotting (e.g., vitamin K) may be useful in some cases
 - Intravenous fluid replacement or blood transfusion may be indicated when a large amount of blood has been lost
- 7.5.4 Anesthetic overdose
 - 7.5.4.1 Cause: Improper dose calculations or administration of drug
 - 7.5.4.2 Prevention
 - Knowledge of drugs and animals used
 - Careful monitoring during induction phase
 - 7.5.4.3 Treatment (See 6.1.10)
- 7.6 Incisions
 - 7.6.1 Closure
 - 7.6.1.1 To facilitate wound healing, it is important to match both needle size and suture material type and size to the procedure
 - 7.6.1.2 Multiple layers of sutures placed in an interrupted pattern are preferred to a continuous pattern to minimize the risk of dehiscence
 - 7.6.1.3 A subcuticular suture pattern is advantageous for skin closure in animals that are inclined to chew or otherwise remove stitches
 - 7.6.1.4 Knots used to join the ends of suture material must be tied correctly and securely to prevent spontaneous loosening during the healing process
 - 7.6.1.5 Metal clips can be used in lieu of sutures to close skin incisions in thin-skinned animals
 - 7.6.2 Dehiscence
 - 7.6.2.1 Causes
 - Sutures improperly placed
 - Knots improperly tied
 - Healing compromised by bacterial infection
 - 7.6.2.2 Prevention: Use of good surgical techniques

7.6.2.3 Treatment

- Thorough cleaning of wound, trimming away of unhealthy tissue, and reapplication of sutures
- Use of parenteral antibiotics if infection is present

7.7 Postsurgical Care

- 7.7.1 Trained personnel should observe the animal from the time surgery is completed to the time that the animal has recovered from anesthesia sufficiently to maintain itself in sternal recumbancy
- 7.7.2 The animal should be kept warm, quiet, and clean throughout the immediate postoperative period to facilitate the metabolism of anesthetic and to maximize healing of the incision
- 7.7.3 Supplemental fluids, analgesics, and other drugs should be scheduled in the protocol and administered as needed
- 7.7.4 Special diets, housing, and environmental conditions (e.g., temperature, humidity) should be considered to maximize the rate of healing
- 7.7.5 If large volumes of balanced electrolytes or other fluids are administered subcutaneously, the injections should be made at multiple sites to prevent tissue damage
- 7.7.6 Antibiotics should be used only when needed to treat postoperative infections; they must be carefully selected to avoid specific species intolerances
- 7.7.7 Remove sutures at the appropriate time
- 7.7.8 Notes on daily monitoring of the animal's progress, administration of medicaments, and management of the surgical incision up to the time of suture removal should be recorded on the clinical record
- 7.7.9 The development of the postoperative care protocol should be done in consultation with and under the supervision of the attending veterinarian
- 7.7.10 A kit containing a variety of drugs and equipment that may be needed in a medical emergency should be available in the immediate postoperative care area

7.8 Equipment: Type needed to properly support surgical procedures is dependent on a number of variables, including the species of animal used, the nature of the procedure, and the anesthetic agent used

- 7.8.1 Circulating water heating pads and heatlamps are helpful for preventing hypothermia
- 7.8.2 Nebulized liquids are helpful in relieving pulmonary congestion
- 7.8.3 Vacuum (suction) equipment is useful for removing accumulations of mucus from the respiratory tract and fluid from body cavities
- 7.8.4 Oxygen administration facilitates the return of normal pulmonary function and increases the rate of tissue healing
- 7.8.5 A mechanical respirator (ventilator) should be available to support respiration when the animal's system is compromised, and the animal is unable to breathe normally
- 7.8.6 A cardiac monitor is essential for evaluating heart rate and pattern
- 7.8.7 An electronic thermometer is helpful for monitoring body temperature

- 7.8.8 A mechanical gas anesthesia machine or an airtight chamber is essential for the administration of volatile anesthetics, and some form of gas-scavenging system should be provided to remove excess gas from the room
- 7.8.9 An electrocautery unit is useful for managing hemostasis during surgery
- 7.8.10 An esophageal stethoscope is useful for monitoring heart beat during surgery
- 7.9 Recordkeeping
 - 7.9.1 A permanent record should be established for each animal undergoing surgery
 - 7.9.2 The record should be complete, current, and readily accessible
 - 7.9.3 A brief description of the surgical procedure should be recorded and should reflect what was approved by the IACUC
 - 7.9.4 Any unexpected or abnormal reaction to anesthetics or other drugs should be recorded
 - 7.9.5 Any information that might be of value or assistance for maintaining the animal after surgery should be recorded
 - 7.9.6 All postsurgical care provided should be documented

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8

Euthanasia

8.1 Definition

- 8.1.1 A method of killing an animal that ensures minimal physical and psychological suffering (AVMA, 1986)
- 8.1.2 A process of killing that renders the animal unconscious (and thus insensitive to pain) as rapidly as possible, without fear and anxiety (CCAC, 1980)

8.2 Legal Requirements

- 8.2.1 AWRs (9 CFR 1.1, 2.31)
 - 8.2.1.1 Method must produce rapid unconsciousness and subsequent death without evidence of pain or distress; or
 - 8.2.1.2 Method must utilize anesthesia produced by an agent that causes painless loss of consciousness and subsequent death
- 8.2.2 PHS policy (PHS, 1986)
 - 8.2.2.1 Method must be consistent with the recommendations of the American Veterinary Medical Association Panel on Euthanasia (AVMA, 1986, or succeeding revised editions); or
 - 8.2.2.2 If method deviates from AVMA recommendations, the deviation must be justified scientifically and approved by the institutional animal care and use committee (IACUC)
- 8.2.3 Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly killed at the end of the procedure, or if appropriate, during the procedure (9 CFR 2.31; PHS, 1986)
- 8.2.4 Attending veterinarians are responsible for providing guidance to principal investigators and other personnel (9 CFR 2.31)

- 8.2.5 Institutions must ensure that personnel are appropriately trained and qualified in the methods of euthanasia that will be used (9 CFR 2.31)
- 8.3 Ethical and Humane Considerations
 - 8.3.1 Euthanasia should be performed quickly and efficiently in a nonpublic area but not in rooms in which animals are housed
 - 8.3.2 Criteria should be developed for deciding when the level of pain and distress is such that euthanasia is warranted, and the person responsible for making that decision should be identified in the experimental protocol (Ad Hoc Committee on Animal Research, 1988; Everitt and Griffin, 1988)
 - 8.3.2.1 Moribund animals: An acceptable endpoint should be determined, consistent with sound research design, so that suffering is not prolonged unnecessarily
 - 8.3.2.2 Animals with solid tumors should be killed when
 - The size of the tumor interferes with normal behavior such as eating, drinking, and freedom of movement
 - The tumor ulcerates or develops necrotic areas
 - Clinical signs such as weight loss, lethargy, and inappetence appear (for tumors that are not palpable)
 - 8.3.3 Euthanasia-associated pain and distress should be prevented or minimized in nervous or intractable animals by skillful handling or by the administration of tranquilizers, sedatives, or analgesic drugs
 - 8.3.4 A person performing euthanasia should demonstrate professionalism and sensitivity for the value of animal life
 - 8.3.5 Death should be confirmed by checking for the absence of a heartbeat; the absence of respiration does not always indicate death
- 8.4 Human Considerations
 - 8.4.1 Euthanasia is often a stressor to the person performing the procedure
 - 8.4.1.1 To many people, the taking of an animal's life is an awesome task
 - 8.4.1.2 The degree of distress experienced by those people observing or performing euthanasia or death in any form is dependent on their backgrounds and on their personal philosophies and ethical concerns about using animals in research (Arluke, 1988)
 - 8.4.1.3 Because of the kinship between people and higher animals, however distant, the unpleasant reaction people have to human death is often transferred to the death of animals
 - 8.4.1.4 The stress of performing euthanasia is magnified when there are strong emotional bonds between personnel and individual animals or when large numbers of animals are killed on a regular basis
 - 8.4.1.5 The stress experienced by people who regularly perform euthanasia may cause a strong sense of work dissatisfaction or alienation, which might be expressed by absenteeism, belligerence, or careless and callous handling of animals, along with a high turnover rate of personnel
 - 8.4.2 Coping effectively with euthanasia-associated emotional stress

- 8.4.2.1 Supervisory awareness and sensitivity must be developed
- 8.4.2.2 Coping skills for employees should be developed through institutional and other programs in stress management and coping with death and dying
- 8.4.2.3 Personnel should be taught the facts about euthanasia
 - The effects of various agents and methods are subjective and based on professional judgment, experience, and intuition
 - Some of the reported disadvantages and controversy about certain practices are based on sentiment and aesthetic considerations rather than on sound scientific data
 - Some physical methods may be aesthetically unpleasant but quite humane
 - The choice of a method for euthanasia must be based primarily on humane concerns rather than on the sensitivities of the technician who performs or the people who observe the euthanasia
 - Involuntary movements and vocalization can occur after an animal is unconscious and do not necessarily indicate that the animal is feeling pain

8.5 Criteria for Selection of Method of Euthanasia

- 8.5.1 Has a rapid, initial depressive action on the central nervous system so that the animal is quickly rendered unconscious and insensitive to pain
- 8.5.2 Is appropriate for the age, species, and health of the animal
- 8.5.3 Does not cause fear, anxiety, or panic in the animal being killed or in other animals in the room
- 8.5.4 Produces nonreversible effects
- 8.5.5 Is compatible with the requirements and purpose of a study and does not interfere with postmortem evaluation
- 8.5.6 Is safe for operators and observers to use, causes minimal emotional stress, and has little potential for abuse
- 8.5.7 Is available and economically feasible to use

8.6 Pharmacologic Methods

8.6.1 Inhalant agents

8.6.1.1 General

- Mode of action: Air in lungs is displaced by inhalant agent, and hypoxia of the brain or anesthesia and loss of consciousness follow
- Advantage: Particularly valuable in animals in which venipuncture is difficult (e.g., birds, rodents, cats, small dogs)
- Disadvantages
 - Vapors can be irritating and induce excitement
 - Exposure to vapors can be harmful to personnel and to other animals (a gas-scavenging system or fume hood is necessary)
 - Newborn animals are accustomed to low oxygen and are more resistant to inhalant agents

- 8.6.1.2 Halothane, methoxyflurane, and nitrous oxide
- Mode of action: Central nervous system (CNS) depression
 - Advantage: Nonflammable and nonexplosive under ordinary environmental conditions
 - Disadvantage: Relatively expensive; impractical for routine use
- 8.6.1.3 Chloroform: Not recommended for use
- Mode of action: CNS depression
 - Disadvantages:
 - Is a potent hepatotoxin and a suspected carcinogen
 - Can produce phosgene gas in the presence of a flame
- 8.6.1.4 Nitrogen
- Mode of action: Displaces oxygen and produces death by hypoxia
 - Advantage: Constitutes a minimal hazard to humans because it mixes easily with room air
 - Disadvantages
 - Does not kill very young animals rapidly
 - Manner of death may be aesthetically objectionable
- 8.6.1.5 Carbon monoxide (CO)
- Mode of action: Displaces oxygen on hemoglobin and produces death by hypoxia of the brain
 - Advantages
 - Induces rapid death without pain or discernible discomfort
 - Acceptable for small animals, including dogs and cats, provided that precautions are taken as prescribed by the AVMA Panel on Euthanasia (AVMA, 1986)
 - Disadvantages
 - If generated by gasoline combustion engines, CO must be filtered and cooled to prevent discomfort to the animals
 - CO gas is hazardous to personnel
- 8.6.1.6 Carbon dioxide (CO₂): Not approved for euthanasia in some states
- Mode of action: Hypoxia of the brain
 - Advantages
 - Well accepted and commonly used for euthanasia
 - Discomfort of hypoxia is easily reduced by adding oxygen (30% O₂, 70% CO₂)
 - Inexpensive, nonflammable, and nonexplosive
 - Presents minimal hazard to personnel when used with properly designed equipment
 - Causes no accumulation of chemical residues in tissues
 - Does not distort cellular architecture
 - Is effective for small laboratory animals (e.g., rodents; small or young dogs, cats, and swine; poultry)
 - Disadvantages

- CO₂ is heavier than air so incomplete filling of a euthanasia chamber may permit tall or climbing animals to avoid exposure to the gas
- Time for euthanasia may be substantially prolonged in newborn animals that are more resistant to hypoxia

8.6.1.7 Ether (diethyl ether)

- Mode of action: Hypoxia of the brain
- Advantage: Quick and efficient
- Disadvantages
 - Flammable and explosive
 - Special precautions are required not only while the agent is being used, but also in disposing of dead animals, whose fur and tissue retain gas that continues to vaporize and to constitute a hazard

8.6.2 Noninhalant pharmacologic agents

8.6.2.1 General

- Vary widely in chemical composition
- Death can be induced by multiple routes
 - Intravenous administration is preferred because the effect is the most rapid and reliable
 - Intrapulmonic injection should be avoided because of discomfort to the animals
 - Oral, rectal, and intraperitoneal routes of administration are inadvisable because of prolonged onset of action, wide range in lethal doses, and potential irritation of tissues
 - Intracardiac route is not recommended except in anesthetized or comatose animals
 - Intrathecal route is not recommended except in anesthetized animals
- Excitable and vicious animals should be pretreated with an opioid analgesic, a tranquilizer, or another depressant

8.6.2.2 Barbiturates

- Mode of action: Central nervous system depression
- Advantage: Rapid euthanasia with minimal discomfort, depending on the dose of agent and route of injection (intravenously is preferred)
- Disadvantage: Must be used under supervision of personnel registered with the U.S. Drug Enforcement Agency

8.6.2.3 Chloral hydrate: Not recommended for use by itself

- Mode of action: CNS depression
- Disadvantage: Causes aesthetically objectionable animal movements; therefore, is not recommended for dogs, cats, or other small animals

8.6.3 Drugs that should never be used alone for euthanasia

8.6.3.1 Magnesium sulfate: Lacks analgesic or anesthetic effects

- 8.6.3.2 Potassium chloride: Lacks analgesic or anesthetic effects
- 8.6.3.3 Curariform drugs: Animals remain fully conscious until they suffocate
- 8.6.4 Drugs that should never be used for euthanasia
 - 8.6.4.1 Strychnine: Excites the central nervous system; animal remains conscious until it dies from suffocation
 - 8.6.4.2 Nicotine: Produces serious side effects before death
 - 8.6.4.3 Hydrocyanic acid: Extremely hazardous to humans
- 8.7 Physical Methods
 - 8.7.1 General characteristics
 - 8.7.1.1 Cause immediate loss of consciousness through physical trauma to the brain or spinal cord
 - 8.7.1.2 Users must be thoroughly trained, because improper performance of the procedures may cause the animal severe pain or distress
 - 8.7.1.3 Have a high potential for being aesthetically displeasing to observers
 - 8.7.1.4 Are most useful when pharmacologic methods would interfere with the purpose of the experiment
 - 8.7.2 Penetrating captive bolt
 - 8.7.2.1 Irreversibly damages the cerebral hemisphere and brainstem
 - 8.7.2.2 Advantages
 - Does not chemically contaminate tissues
 - Causes immediate unconsciousness
 - Humane method for use in large animals such as horses, ruminants, and swine when followed by exsanguination or pithing
 - 8.7.2.3 Disadvantages
 - Aesthetically displeasing
 - Improper technique is highly likely to injure the animal and cause pain
 - 8.7.2.4 Nonpenetrating captive bolt pistols are not recommended for use
 - 8.7.3 Gunshot
 - 8.7.3.1 Advantage: Death is instantaneous when the method is performed by a competent person
 - 8.7.3.2 Disadvantages
 - May be dangerous to personnel
 - Aesthetically displeasing—should be used only in emergencies; under circumstances where other methods might not be readily usable, such as in field studies; or for farm animals in rural locations
 - 8.7.4 Stunning
 - 8.7.4.1 Humane only when the procedure is properly performed
 - 8.7.4.2 Must be followed by some other means (e.g., exsanguination, decapitation, thoracotomy) to ensure death
 - 8.7.4.3 Difficult to ensure consistency of effect in rabbits, rodents, and other small laboratory animals
 - 8.7.4.4 Should be evaluated by the IACUC on a case-by-case basis

- 8.7.5 Cervical dislocation
 - 8.7.5.1 When performed properly, it is a humane technique for euthanasia of poultry, mice, and immature rats and rabbits
 - 8.7.5.2 Recommended that animals be sedated or lightly anesthetized beforehand, because they may not lose consciousness immediately (AVMA, 1986)
 - 8.7.5.3 Requests to use this method should be reviewed by the IACUC on a case-by-case basis
- 8.7.6 Decapitation by guillotine
 - 8.7.6.1 Used most often for euthanasia of rodents and small rabbits because they can be restrained without undue stress
 - 8.7.6.2 Animals should be sedated or lightly anesthetized before guillotining or their severed heads should be immersed immediately in liquid nitrogen because it is not known whether there is immediate loss of consciousness
 - 8.7.6.3 Advantage: Facilitates collection of brain tissue that is not contaminated with extraneous chemicals
- 8.7.7 Pithing
 - 8.7.7.1 Effective for killing some poikilotherms (e.g., reptiles, amphibians)
 - 8.7.7.2 Both brain and spinal cord must be pithed
 - 8.7.7.3 Should be conducted only by trained personnel
- 8.7.8 Exsanguination: Animals should be sedated, stunned, or anesthetized because of the anxiety associated with extreme hypovolemia
- 8.7.9 Focused beam microwave irradiation
 - 8.7.9.1 Humane for small laboratory rodents if done with a special microwave apparatus that focuses the energy on the brain to produce immediate unconsciousness
 - 8.7.9.2 Microwave instrument must provide adequate kilowattage
 - 8.7.9.3 Microwave ovens designed for domestic and institutional kitchens should never be used for euthanasia
 - 8.7.9.4 Advantage: Fixes chemical activity of brain tissue
- 8.7.10 Rapid freezing by immersion in liquid nitrogen
 - 8.7.10.1 To be used only for animals weighing 40 gms or less because larger animals are not rendered unconscious rapidly
 - 8.7.10.2 Requires well-trained personnel and appropriate equipment
 - 8.7.10.3 Advantage: Instantaneously inactivates and fixes enzymes in brain tissue
- 8.7.11 Air embolism: Not recommended for routine use
 - 8.7.11.1 Intravenous injection of 5 to 50 ml/kg of air induces rapid death in rabbits
 - 8.7.11.2 Acceptable method only when animals are anesthetized
- 8.7.12 Physical methods not recommended for use
 - 8.7.12.1 Decompression (hypoxia): Induces unconsciousness and death due to cerebral edema

8.7.12.2 Electrocution

- Requires special equipment that passes electrical current directly through the brain to cause immediate loss of consciousness
- Is potentially hazardous to personnel

8.8 Carcass Disposal

8.8.1 Conduct the process in a way that demonstrates respect for the animal

8.8.2 Occupational hazards

8.8.2.1 Evaluate possible hazards to human handlers when animals are known to be carrying a zoonotic agent or were treated with radioisotopes or toxic chemicals

8.8.2.2 Ensure that personnel handling such carcasses take the necessary precautions to protect themselves and others

8.8.3 Follow institutional guidelines for packaging carcasses and moving them to the incinerator to ensure proper disposal

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- Code of Federal Regulations, Title 9 (Animals and Animal Products), Subchapter A (Animal Welfare), Parts 1-3. Copies available from: Animal Care Staff, Regulatory Enforcement and Animal Care, Federal Building, Room 268, Hyattsville, MD 20782.
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- PHS (Public Health Service). 1986. *Public Health Service Policy on Humane Care and Use of Laboratory Animals*. Washington, D.C.: U.S. Department of Health and Human Services. 28 pp. Copies available from: Office for Protection from Research Risks, Building 31, Room 4B09, National Institutes of Health, Bethesda, MD 20892.

9

Husbandry, Care, and the Importance of the Environment

9.1 Legal Requirements for Husbandry and Care

9.1.1 Animals covered

9.1.1.1 AWRs: Any warmblooded animal used or intended for use in research, testing, or education except birds, rats of the genus *Rattus* and mice of the genus *Mus* bred for use in research, and horses and other farm animals used or intended for use in agricultural research and production (see 9 CFR 1.1)

9.1.1.2 PHS Policy: All live vertebrates used in PHS-conducted or supported activities

9.1.1.3 State and local laws, as applicable

9.1.2 Scope of Coverage

9.1.2.1 Facilities and operating procedures in facilities, including temperature and humidity, lighting, cage construction and maintenance, cage size, and waste disposal

9.1.2.2 Animal health and husbandry, including feeding, watering, sanitation, staffing, classification and separation, and veterinary care

9.1.2.3 Transportation, including construction, size, and ventilation of transportation cage; identification of animals; and care in transit

9.2 Importance of Proper Husbandry and a Stable Environment

9.2.1 Improves validity and reliability of experimental data

9.2.2 Conserves research resources

9.2.2.1 Reduces number of animals necessary

9.2.2.2 Reduces time required to complete experiments

9.2.2.3 Reduces cost

- 9.2.3 Improves staff morale and community relations
- 9.3 Environmental Variables That Can Be Controlled
 - 9.3.1 The micro- and macroenvironments
 - 9.3.1.1 Definitions
 - Microenvironment: The physical environment immediately surrounding the animal, for example, temperature and humidity in the cage or primary enclosure (NRC, 1985)
 - Macroenvironment: The physical conditions in the room or secondary enclosure (NRC, 1985)
 - 9.3.1.2 Importance of the microenvironment
 - Profoundly affects metabolism, behavior, and susceptibility to diseases
 - May vary greatly from macroenvironment, depending on cage design (e.g., ammonia levels will be higher in an enclosed cage than in an open one)
 - Can be more difficult to monitor and regulate than the macroenvironment
 - 9.3.2 Examples of variables that can affect animal health and research outcomes
 - 9.3.2.1 Temperature and humidity
 - 9.3.2.2 Ventilation
 - 9.3.2.3 Population density
 - 9.3.2.4 Illumination
 - 9.3.2.5 Noise (frequency, loudness, suddenness of onset)
 - 9.3.2.6 Food and water
 - 9.3.2.7 Type of bedding
 - 9.3.2.8 Sanitation
 - 9.3.2.9 Handling (age of animal, frequency of handling)
- 9.4 Dealing with Emergencies (e.g., power failure, flooding, air-handling failure, heating or cooling failure, fire)

REFERENCE

- NRC (National Research Council). 1985. *Guide for the Care and Use of Laboratory Animals*. A report of the Institute of Laboratory Animal Resources Committee on Care and Use of Laboratory Animals. NIH Pub. No. 86-23. Washington, D.C.: U.S. Department of Health and Human Services.

10

Species-Specific Overview

The following outline is intended as a guide for preparing a series of programs, each designed to provide information on a specific animal (e.g., dogs, nonhuman primates) or group of animals (e.g., rodents). Topics are broken down by animal type only in those instances in which the material to be covered depends on animal type. With the exception of the Specific Techniques section, which is intended to be hands-on training, the material in this section can be presented in a variety of formats, as appropriate to institutional needs and constraints.

OUTLINE

10.1 Factors Associated with Selection of Animals

10.1.1 Rodents

10.1.1.1 Types of stocks

- Inbred: Each animal of the strain is virtually genetically identical to all the others of that strain
- Hybrid: The first generation offspring of two inbred strains; known genetic background, but heterozygous at most loci
- Mutant: Each animal carries an inherited trait or a combination of traits that allows the study of a specific biologic process or disease
- Outbred: Genetics unknown; very heterogeneous
- Other specialized stocks (e.g., transgenic animals)

10.1.1.2 Standardized nomenclature

- Importance of using standardized nomenclature
- Sources for rules of standardized nomenclature (International Committee on Laboratory Animals, 1972; Lyon and Searle, 1989; Greenhouse, in press)

10.1.1.3 Microbiologic status

- Effects of clinical and subclinical infections on research outcomes (NRC, in press a,b)
- Definitions of terms describing microbial status (NRC, in press a)
 - Germfree: A hysterectomy-derived animal that has been reared and maintained in an isolator by germfree techniques and demonstrated free of associated forms of life, including viruses, bacteria, fungi, protozoa, and other saprophytic or parasitic forms
 - Gnotobiot: A hysterectomy-derived animal that has been reared and maintained in an isolator by germfree techniques and that has one or more associated nonpathogenic agents, all of which are known
 - Defined flora: A germfree animal that has been intentionally associated with one or more microorganisms and maintained continuously in an isolator to prevent contamination by other agents (term may be used synonymously with gnotobiot)
 - Pathogen free: An animal free of all demonstrable pathogens; proper usage of the term requires that the pathogen-free status be supported by current results from a battery of tests appropriate for all pathogens of a specific species (term differs little from specific pathogen free)
 - Specific pathogen free (SPF) or barrier maintained: An animal free of a specified list of pathogens; proper usage of the term requires that the absence of the specified pathogens be supported by current test results from a battery of tests appropriate for those pathogens
 - Virus antibody free: An animal free of antibodies to viral pathogens; proper usage requires that the absence of viral pathogens be supported by current test results from a battery of appropriate serologic tests
 - Clean conventional: An animal housed in a low-security barrier and demonstrated to be free of major pathogens
 - Conventional: An animal whose microbial burden is not known and not controlled; the animal is generally housed in open rooms with unrestricted access
- Animal resource policy

- 10.1.2 Rabbits
 - 10.1.2.1 Breeds
 - 10.1.2.2 Microbiologic status
- 10.1.3 Dogs and cats
 - 10.1.3.1 Breeds
 - Purebred
 - Mixed breed
 - 10.1.3.2 Purpose bred or random source
 - Availability
 - Health and vaccination history
- 10.1.4 Nonhuman primates
 - 10.1.4.1 Genus and species
 - 10.1.4.2 Colony-born, wild-caught, or previously used in experimentation
 - Availability
 - History (e.g., date of birth)
 - Health records
 - Previous experimental procedures
- 10.1.5 Other animals (as appropriate to the audience)
- 10.2 Procurement of Animals
 - 10.2.1 Information on sources of animals
 - 10.2.1.1 Institutional animal resource
 - 10.2.1.2 Institute of Laboratory Animal Resources
 - 10.2.1.3 Primate Information Clearing House
 - 10.2.2 Requirements for purchasing animals
 - 10.2.2.1 Legal requirements
 - Dogs and cats
 - Threatened or endangered species
 - 10.2.2.2 Institutional requirements
 - Requirement for purchasing only from USDA-licensed dealers, if applicable
 - Microbiologic status
 - Health records
 - Quarantine and stabilization
- 10.3 Caging
 - 10.3.1 Types of caging regularly available in the institution
 - 10.3.1.1 Advantages and disadvantages
 - Species needs
 - Safety (people and animals)
 - Security
 - Visibility
 - Accessibility
 - Disease control
 - Sanitation

- 10.3.1.2 Maximum population density permitted
 - Size of individuals
 - Age of individuals
 - Aggressive animals
 - Physiologic and metabolic signs of overcrowding
 - Increased corticosterone levels
 - Loss of fertility
 - Behavioral effects of overcrowding
 - Aggression
 - Cannibalism
 - Self-mutilation
- 10.3.2 Special caging
 - 10.3.2.1 Metabolic
 - 10.3.2.2 Intensive care or therapy
 - 10.3.2.3 Special construction
- 10.4 Environmental Enrichment
 - 10.4.1 Legal requirements
 - 10.4.1.1 Dogs
 - 10.4.1.2 Nonhuman primates
 - 10.4.2 Institutional policies
 - 10.4.3 Group housing and socialization
 - 10.4.4 Special equipment
- 10.5 Food
 - 10.5.1 Advantages and disadvantages of food-delivery methods available
 - 10.5.1.1 Appropriateness for age of animal
 - 10.5.1.2 Appropriateness for health status of animal
 - 10.5.1.3 Adequate availability for all individuals in a social group (subordinates are not food deprived)
 - 10.5.2 Nutrition
 - 10.5.2.1 Supplementation of standard diets available
 - 10.5.2.2 Diet control
 - Batch date
 - Frequent content assessment
 - 10.5.2.3 Special dietary needs
 - Unusual amounts of food, such as for pregnant and nursing animals
 - Special types of food
 - Caloric restriction
 - 10.5.2.4 Availability and sources of experimental diets
 - 10.5.3 Delivery of experimental agents
 - 10.5.4 Food deprivation carried out under approved experimental protocol
- 10.6 Water
 - 10.6.1 Advantages and disadvantages of available water delivery methods

- 10.6.2 Delivery of experimental agents
- 10.6.3 Water deprivation carried out under approved experimental protocol
- 10.7 Handling and Restraint
 - 10.7.1 Regulations and policies
 - 10.7.2 Importance of proper handling (cite examples)
 - 10.7.2.1 Avoid injury to animals
 - 10.7.2.2 Avoid injury to personnel
 - 10.7.2.3 Minimize stress
 - 10.7.2.4 Aesthetics
 - 10.7.3 Techniques for handling
 - 10.7.4 Methods of restraint
 - 10.7.4.1 Physical
 - 10.7.4.2 Chemical
 - 10.7.4.3 Mechanical
 - 10.7.5 Prolonged restraint
 - 10.7.5.1 Regulations and policies
 - 10.7.5.2 Procedures to reduce stress
 - Selection of the least restrictive system compatible with research objectives
 - Selection of the minimal restraint time needed to accomplish the research objectives
 - Conditioning of animals to restraint devices before beginning research
 - Prevention or treatment of problems resulting from restraint, including contusions, decubital ulcers, dependent edema, weight loss, and traumatic injury
- 10.8 Identification and Records
 - 10.8.1 Legal requirements
 - 10.8.1.1 PHS policy (*Guide for the Care and Use of Laboratory Animals*) (NRC, 1985)
 - 10.8.1.2 Animal welfare regulations (9 CFR 2.35): Dogs and cats
 - 10.8.1.3 Good Laboratory Practices (21 CFR 58.90)
 - 10.8.2 Advantages and disadvantages of identification methods: Tattoos, color or dye markings, natural markings, ear punch, toe clipping, ear tags, collars
 - 10.8.3 Recordkeeping
 - 10.8.3.1 Cage card: Species and strain of animals, sex, weights, source, identification number, responsible investigator, other pertinent data
 - 10.8.3.2 Individual identification: Species and strain or breed of animal, source
- 10.9 Animal Health
 - 10.9.1 Normal parameters
 - 10.9.1.1 Life cycle
 - 10.9.1.2 Behavior patterns, including reproduction

- 10.9.1.3 Physiologic parameters
- 10.9.1.4 Clinical chemistry
- 10.9.2 Health surveillance
 - 10.9.2.1 Importance of the health-surveillance program
 - Minimizes pain and discomfort associated with disease, injury, or distress
 - Reduces number of animals required by minimizing loss
 - Improves the reliability and validity of experimental data
 - Enables early intervention in cases of disease and injury
 - Reduces probability of spread of disease
 - 10.9.2.2 Role of the research team
 - Assists in detection of distress and disease through frequent observation
 - Reports signs of distress and disease to veterinary staff and consults on plan of action
- 10.9.3 Signs of distress and disease
 - 10.9.3.1 Gross signs
 - Cutaneous: Alopecia, cutaneous or subcutaneous swelling, dermatitis, abnormal hair coat, necrosis, discoloration
 - Gastrointestinal: Diarrhea, constipation, cramping (hunched posture), anorexia, ptialism, rectal prolapse, pendulous abdomen
 - Respiratory: Dyspnea, abnormal respiratory sounds, nasal and ocular discharges
 - Urinary: Polydipsia, excessive or reduced volume, content or color abnormalities, unusual odor, straining to urinate
 - Neuromuscular and skeletal: Paresis or paralysis, seizures, torticollis, incoordination, lameness
 - Reproductive: Infertility, abortions, discharges, still births, litter desertion, orchitis, mastitis
 - Miscellaneous: Unexpected deaths, loss of appendages, weight loss, anemia, eye lesions
 - 10.9.3.2 Physiologic signs
 - Blood: Anemia; cell size, count, or type
 - Urinary: Abnormalities in specific gravity, color, content, chemistry, volume, odor
 - Decreased or elevated body temperature, pulse or respiratory rate
 - Miscellaneous: Changes in synovial or cerebrospinal fluids, nerve impulse transmission, bone density, liver and pancreatic function, endocrine function, mineral and pH balance
 - 10.9.3.3 Behavioral signs
 - Inappetance
 - High or low levels of activity

- Withdrawal to a cage corner
 - Inter- or intraspecies aggression
 - Unusual or repetitive movement patterns
 - Excessive self grooming
 - Sexual and maternal abnormalities
 - Self-mutilation
- 10.9.4 Common diseases
- 10.9.4.1 Rodents
- Mice: Acariasis, pneumonias, abscesses, mammary neoplasia, subclinical viral infections such as MHV and Sendai
 - Rats: Incisor malocclusion, chronic respiratory disease, mammary (benign) neoplasia, nephrosis, sialodacryoadenitis, chromodacryorrhea, moist dermatitis
 - Guinea pigs: Pneumonia, enteropathies, dermatophytosis, hypovitaminosis C, premolar malocclusion, mastitis, pregnancy toxemia, pediculosis, urolithiasis, limb fractures
 - Hamsters: Demodecosis, renal amyloidosis, limb fractures, enteropathies, cutaneous and adrenal neoplasia
- 10.9.4.2 Rabbits: Otic acariasis, coccidiosis, enteropathies, malocclusion, lumbar fracture, moist dermatitis, pasteurellosis, ulcerative pododermatitis
- 10.9.4.3 Dogs: *Bordetella* infection; distemper; parvovirus infection; herpesvirus infection; heartworms; intestinal and cutaneous parasitism; hepatitis, adenovirus, and parainfluenza infections; neoplasia
- 10.9.4.4 Cats: Infectious peritonitis, panleukopenia, respiratory disorders, toxoplasmosis, parasitism, leukemia, urologic syndrome, otic acariasis
- 10.9.4.5 Nonhuman primates: Enteropathies, tuberculosis, trauma, caloric insufficiency, hypovitaminosis C or D₃, herpesvirus infections
- 10.9.4.6 Other animals: Include as appropriate to audience
- 10.9.5 Experimentally produced disorders: Physical, electrophysiologic, microbiologic, or chemical alteration of any part so as to produce an abnormal sign; must be differentiated (based on history) from signs associated with spontaneous diseases
- 10.9.6 Institutional procedures for emergency or special care
- 10.10 Zoonoses (Describe signs and symptoms in animals and humans)
- 10.10.1 Types
- 10.10.1.1 Naturally occurring
- Rodents: Lymphocytic choriomeningitis, rat-bite fever, Korean hemorrhagic fever and related diseases (animals imported from Europe and Asia)
 - Dogs: Rabies, brucellosis, ringworm, endoparasite-induced disease

- Cats: Cat-scratch fever, toxoplasmosis, endoparasite-induced disease
 - Nonhuman primates: Tuberculosis, herpesvirus B infection, Marburg disease, infectious hepatitis, monkeypox
 - Ungulates: Encephalomyelitis, Q fever, leptospirosis, tetanus, contagious ecthyma, cowpox
 - Birds: Psitticosis (ornithosis), salmonellosis, encephalomyelitis
 - Wild rodents/racoons: Rat bite fever, tularemia, plague, rabies
- 10.10.1.2 Experimentally produced (any agent injected, fed, or introduced by biotechnology)
- 10.10.2 Techniques for handling animals carrying or at high risk for carrying zoonotic agents
- 10.11 Specific Techniques: Hands-on training in techniques such as blood withdrawal, injections, specimen collection, measurement of vital signs, and euthanasia

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IV
RESOURCES

1

Sources of Information

The following organizations are useful resources for course coordinators, content experts, and participants.

Animal Welfare Information Center

See Appendix II. Contact: Animal Welfare Information Center, National Agricultural Library, Room 304, Beltsville, MD 20705 (301-344-3212).

National Library of Medicine

Maintains an extensive collection of published source materials and reference works on basic veterinary sciences and clinical veterinary medicine, emphasizing those areas most closely related to human health and health research. Publishes *Current Bibliographies in Medicine*, including those dealing with pain, anesthesia, and analgesia in laboratory animals; care and use of animals; and laboratory animal welfare. Contact: National Library of Medicine, Coordinator of Veterinary Affairs, Bethesda, MD 20892 (301-496-6308).

Institute of Laboratory Animal Resources

Provides information on sources of laboratory animals and appropriate animal models for studying physiologic and pathologic processes. Prepares guidelines for the care and use

of laboratory animals. Contact: Institute of Laboratory Animal Resources, National Research Council, 2101 Constitution Avenue, Washington, DC 20418 (202-334-2780).

Foundation for Biomedical Research

Provides information for the scientific community and the general public on the use of animals in research, testing, and education. Provides a handbook and training materials. Contact: Foundation for Biomedical Research, 818 Connecticut Avenue, NW, Suite 303, Washington, DC 20006 (202-457-0654).

Center for Alternatives

Disseminates information on alternatives to the use of animals in product safety testing. Publishes a newsletter three times per year on progress in *in vitro* toxicology, distributes reprints of scientific articles by the director and associate director, and provides technical reports in *in vitro* toxicology. Contact: Center for Alternatives, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD 21205 (301-955-3343).

Center for Animals and Public Policy

Analyzes technical and public policy issues relating to the development and application of alternatives to laboratory animals in toxicity testing. Provides a bimonthly technical newsletter containing news and analysis on the latest developments in the search for alternatives; the relevant policy issues; and the roles of government, industry, and the public. Conducts and provides reports of workshops for various interest groups involved with the alternatives issue. Contact: Center for Animals and Public Policy, Tufts University School of Veterinary Medicine, 200 Westboro Road, North Grafton, MA 01536 (508-876-5302, Ext. 4750).

2

Selected Bibliography

The following selected bibliography is provided to assist those who present course topics in preparing their material. It can also be used as a resource for participants. The references that the committee believes are essential for a minimum institutional library have been designated by an asterisk.

A publication that summarizes many of the areas covered in this program is as follows:

- *Essentials for Animal Research. A Primer for Research Personnel.** B. T. Bennett, M. J. Brown, and J. C. Schofield. 1990. Beltsville, Md.: National Agricultural Library. 126 pp.

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- *Good Laboratory Practices Regulations.**
- Code of Federal Regulations, Title 21 (Food and Drugs), Part 58 (Good Laboratory Practice for Nonclinical Laboratory Studies), Subparts A-K.
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3

Audiovisual Materials

No single reference includes all audiovisual materials that might in some way relate to the care and use of laboratory animals. The following organizations, however, publish catalogs that provide information on content, format, and costs of most programs available:

American Association for Laboratory Animal Science (AALAS). Publishes a catalog of slide-tape, film, and computer disc programs on all aspects of laboratory animal care and use. Maintains slide programs, primarily for training postdoctoral veterinary students, which are loaned free to members and for a fee to nonmembers. Contact: AALAS, 70 Timber Creek Drive, Cordova, TN 38018 (901-754-8621).

American Venterinary Association (AVMA). Publishes the *Veterinary Audiovisual Catalog*, which lists programs relevant to veterinary medicine. Maintains library of films and videotapes that are loaned to members free-of-charge. Contact: AVMA, 930 North Meacham Road, Schaumburg, IL 60196 (800-248-2862).

Atlantic Provinces Council on the Sciences, Animal Care Committee. Published a catalog, compiled by William Threlfall (1989), entitled *Audiovisual Materials Concerning the Care, Use, Behavior and General Biology of Animals*, which contains a reading list and a list of audiovisual materials on a wide variety of subjects and on a large number of animal species. Contact: Dr. William Threlfall, Department of Biology, Memorial University of Newfoundland, St. John's, Newfoundland A1B 3X9, Canada (709-737-7498).

The following institutions maintain and lend or sell audiovisual programs on animal care and use:

- Animal Welfare Institute.** Has books and reprints expressing animal welfare advocate views on animal use and a film on humane care and housing of dogs in an experimental surgery laboratory. Contact: Animal Welfare Institute, P.O. Box 3650, Washington, DC 20007 (202-337-2333).
- Center to Study Human-Animal Relationships and Environments.** Has videotapes on inter-relationships between people and animals, including animal behavior, domestication, human-animal bond, and research use. Contact: CEN/SHARE, University of Minnesota Media Distribution, Box 734 Mayo Building, 420 Delaware Street, SE, Minneapolis, MN 55455 (612-624-7906).
- Foundation for Biomedical Research.** Has videotapes, posters, books, and brochures on the human health benefits of using animals in research. Contact: Foundation for Biomedical Research, 818 Connecticut Avenue, NW, Washington, DC 20006 (202-457-0654).
- Interactive Teleducation Corporation.** Has image-based, computer-assisted interactive training programs on various laboratory animal topics. Contact: Innovative Medical Marketing Associates, 226 Sunny Jim Drive, Medford, NJ 08055 (609-654-5561).
- Iowa State University.** Has a slide programs, videotapes, and films on a variety of topics, including gross and microscopic anatomy and surgical techniques. A catalog is available. Contact: Biomedical Communications, 2261 College of Veterinary Medicine, Iowa State University, Ames, IA 50011 (515-294-6988).
- Laboratory Animal Training Association.** Has videotapes, manuals, and a program that uses both computer programs and videotapes on the humane care and use of laboratory animals and on specific techniques. Contact: Laboratory Animal Training Association, 54 Remington Drive, Suite 301, Highland Village, TX 75067 (800-262-5282).
- MTM Associates, Inc.** Has videotapes and computer programs on basic bi methodology for laboratory animals. Contact: MTM Associates, Inc., P.O. Box 1606, Manassas, VA 22110 (Maryland phone number, 301-731-7360).
- National Agricultural Library.** Has slides, films, and videotapes on care and use of laboratory animals. For a catalog, contact: Animal Welfare Information Center, NAL, Room 205, Beltsville, MD 20705 (301-344-3212). To borrow audiovisual materials, contact: Lending Branch, NAL, Beltsville, MD 20705 (301-344-3755).
- North Carolina State University.** Has two slide/audiotape programs on anatomy, one on mice and rats and another on rabbits. Contact: Dr. James E. Smallwood, Department of Anatomy, Physiology, and Radiology, North Carolina State University, College of Veterinary Medicine, Raleigh, NC 27606 (919-829-4223). Also has videotapes on a variety of surgical and other techniques in animals. Contact: Biomedical Communications, North Carolina State University, College of Veterinary Medicine, Raleigh, NC 27606 (919-829-4489).
- Pennsylvania State University.** Has audiovisual programs on ethology of primates, hamsters, and other species. Contact: Audio-Visual Services, Pennsylvania State University, Special Services Building, University Park, PA 16802 (800-826-0132).
- Southern Illinois University School of Medicine.** Has videotapes on the ethics and use of animals in research. Contact: Southern Illinois University School of Medicine, P.O. Box 19230, Springfield, IL 62794 (217-782-3318).

Texas Tech University Health Sciences Center. Has videotapes on the use of animals in research. Contact: Texas Tech University Health Sciences Center, AV Center, 3601 4th Street, Lubbock, TX 79430 (806-743-2288).

University of California, Davis. Has slide programs and videotapes on techniques using laboratory animals. Contact: Office of the Dean, Instruction, University of California, School of Veterinary Medicine, Davis, CA 95616 (916-752-6521).

University of Florida. Has videotapes on diseases of rabbits and rodents. Contact: Learning Resources Center Television, University of Florida, Box J16, Health Sciences Center, Gainesville, FL 32610-0016. (Make initial contact by phone at 904-392-4143).

University of Washington, Health Sciences Center for Educational Resources. Has slide sets with audiotapes and manuals on laboratory animal science and medicine and on performing a variety of techniques in the common laboratory species. A catalog is available. Contact: HSCER, University of Washington, T-281 Health Sciences SB-56, Seattle, WA 98195 (206-685-1186).

Wisconsin Regional Primate Center. Has slides, audiocassettes, films, and videotapes on nonhuman primate-related topics. Contact: Audio-Visual Services, University of Wisconsin, 1223 Capital Court, Madison, WI 53715-1299 (608-263-3512).

V

HOW TO DEVELOP, DELIVER, AND
EVALUATE AN EDUCATIONAL
PROGRAM

1

How to Approach the Task of Education

EDUCATIONAL GOALS

The goal of education and training in laboratory animal care and use goes far beyond meeting stated requirements of regulating agencies. The intent of the requirement for education is to stimulate changes in knowledge, attitudes, and behaviors that will ensure humane care of animals used in teaching, testing, and research. The education and training methods you select will depend on your audience, the objectives that have been set, and the resources you have available.

Desirable changes in behavior do not automatically follow introduction of information. To help translate knowledge into performance, be sure the learner:

- knows concepts well enough to integrate them into a complex behavioral pattern;
- develops confidence in skills associated with desired behaviors;
- connects rules and associated behaviors with a personal benefit;
- connects principles and rules with practical situations;
- understands when and how to apply information;
- knows the risks of noncompliance;
- has access to services and resources available locally and nationally; and
- receives positive feedback or rewards for the desired behaviors.

Changes in attitudes are stimulated by acquiring information and increasing skills, but they are reinforced by interaction with peers. Therefore, to facilitate a change in attitude the education program for investigators should:

- publicize both institutional and peer support for attending educational programs and for complying with legal requirements;
- encourage questions and discussions;
- build networks; and
- provide a forum for exchanging ideas and expressing concerns.

A final goal of the program should be to document the effectiveness of the institution's approach to training scientists, technicians, and others involved with animal care and use.

SETTING OBJECTIVES

Objectives must be established with a particular audience in mind. A measurable objective is a statement of what the learner should be able to do on completion of a particular educational or training experience. For example, at the end of a lecture, an appropriate goal would be for the learner to demonstrate recall, verbally or in writing. (Note: writing assumes a higher level of competence with language.) A higher level objective would be to ask the participant to apply information to a stated situation or case or to discriminate between situations as to whether a concept applies. Following a lecture and a hands-on laboratory, an appropriate goal would be for the participant to carry out a procedure acceptably, incorporating information and skills. There are three important considerations in setting objectives. First, they must be in line with the outcomes desired. Second, they should be consistent with real-life applications. Finally, the training must provide both the information and the skills to enable the learner to meet the objectives. Desired outcomes are generally increased knowledge or skills to enable performance of a task or changes in attitude that will be reflected in changes in behaviors.

SELECTING METHODS

Once specific subjects are identified for presentation, a variety of educational methods should be considered. Approaches should match the course content to the needs of the learners and to the available resources. Recommended methods include:

- lectures, seminars;
- interactive sessions—discussions with peers: listening teams, problem solving, case studies;
- workshops—demonstrations, wet labs;
- individualized study—readings, videorecordings for home viewing, audiotapes, computerized teaching modules or reviews, audio programs; and
- assessment tools—self-assessment, self-reporting.

Lectures/Seminars

A lecture/seminar format is recommended for presenting most of the introductory, core block of material. This format is suitable for groups of any size, communicates the institutional mandate well, and makes the most efficient use of resources. A session might include several speakers who provide an introduction to the various topics listed. Pre-packaged video or slide programs can be used effectively for portions of the presentation, particularly if the number of content experts is limited.

Interactive Sessions

Provide some interactive experiences during the presentation of the core block, if at all possible. Suggestions for the presentation include the following:

- Provide a panel of experts to address an issue and respond to questions raised by participants (Example: how to write a research protocol that meets the review needs of the institutional animal care and use committee).
- Break a large group into smaller groups for a follow-up discussion of an issue presented (Example: responsibility of the investigator for health and safety of research associates).
- Break a large group into smaller groups in accordance with an interest expressed or a commonality of their work (Example: people whose protocols include pain management or postsurgical monitoring in a particular species).
- Have a structured refreshment break during which participants are asked to introduce themselves to someone they have not met and to discuss an issue (Example: what would you do if you observed another investigator who you felt was not complying with guidelines).

Workshops/Laboratories

A workshop/laboratory is an opportunity to gain hands-on experience. Insofar as possible, labs should be species- or technique-specific, and groups should be kept small. The sessions should provide opportunities for each individual to participate in skill-building activities such as methods of handling animals and performing necessary procedures.

Adult learners, particularly those in a profession, tend to avoid situations in which they cannot demonstrate competence. Therefore, it is usually helpful to introduce the lab with a demonstration, slide show, or video presentation to provide background information. Demonstration with models is also highly recommended prior to hands-on experience. However, media is not a substitute for the hands-on experience needed for developing skills.

The facilitator must be encouraging, positive, and patient toward learners who have little or no prior experience with a particular species of animal or procedure.

Individualized Study

Adult learners appreciate individualized, independent study. A variety of individualized study approaches should be used, including:

- recommended texts;
- reprint files (computerized);
- videotapes, slides, and print visuals;
- computer simulations;
- newsletters to update information, introduce new resources and equipment, and provide reminders of policies;
- checklists and protocols posted in prominent places;
- a "buddy system" in which new investigators are introduced to more experienced researchers, particularly for highly specialized procedures; and
- special-interest or study groups.

Self Assessment

Self-assessment tools are a form of individualized independent study. They provide an investigator with an instrument to test his or her knowledge in a confidential way. This self-assessment tool could be a pencil-and-paper instrument or a computerized program. The essential characteristics are that the results are strictly for the benefit of the person completing the program and that the program identifies areas of weakness. Self-assessment can be combined with self-reporting: a statement that the person has completed the program.

OVERCOMING RESISTANCE TO CHANGE

Some investigators may resent a requirement for education or give the program a low priority. Steps must be taken to overcome potential resistance. Some suggestions are as follows:

- Obtain an endorsement of the program from the highest institutional official and send out letters announcing the program over his/her signature.
- Involve several key people in planning the educational offerings, for example, people

at the institution who represent the needs and views of the researchers, people who have the respect of investigators, or a person from whom resistance is anticipated. Explain the requirements, available resources, and limitations to those people, and encourage them to problem-solve and incorporate their ideas into an action plan. Name these people in publicity about the courses.

- Make compliance with institutional goals as personalized and as easy as possible.
- Develop packets containing species-specific information relating to requirements and guidelines.
- Ensure access to information. Develop reading lists and catalog books and reprint files in the resource library by species and subject for easy access. If a major institutional library will be used as the resource library, arrange for a demonstration on how to locate relevant materials. Develop a "reference bank" of local investigators who have experience with exotic species or are experts in performing advanced techniques.
- Find out from researchers what obstacles to implementation they perceive and develop a mechanism for reducing difficulties in changing behaviors.
- Reward and encourage compliance by acknowledging investigators for their cooperation following successful inspections or accreditation visits. Build a positive image with an active public relations program, such as by displaying articles about research accomplishments.

CONCLUSIONS

A complete education program for researchers and their assistants will:

- disseminate required information
- increase awareness
- improve skills
- affect behaviors
- change attitudes

A well-organized educational program will conserve time and resources, be customized to the content needs of the learners, and be flexible enough to encourage enthusiastic participation.

2

How to Plan and Implement a Training Course

Careful planning and preparation are required to provide informative, well-organized courses. Attention to detail cannot be overemphasized. Up to 6 months should be allowed to organize and implement the first offering of each course.

IDENTIFYING THE TARGET AUDIENCE

Each course must be designed for a specific audience to encourage active participation and achieve desired results. The audience should be defined on the basis of job responsibilities, educational level, experience, motivation, and training needs. This audience profile will help the trainer establish program goals, objectives, content, and presentation method. For example, a program for people who support animal research efforts peripherally, such as security, janitorial, or equipment maintenance personnel, will be designed differently from a program for scientific staff. Likewise, a course for newly hired research staff will include introductory information that may be inappropriate or redundant for staff members who have been employed by the institution for several years.

ALLOCATING A BUDGET/FUNDING

A course budget should be allocated to include honoraria and travel expenses for guest speakers; duplication of handout materials; rental, purchase, or development of audio-visual support materials; room and equipment rental; and costs of publicity.

DETERMINING GOALS AND OBJECTIVES

The goals and learning objectives must be defined clearly during the early phases of course development. As Kemp (1971) has stated, "A good goal is a nonambiguous statement. It means exactly the same thing to all other teachers who use it." Each speaker or course facilitator should be given specific instructional goals for his/her section, which may be communication of information, motivation, or skill building. From these goals, specific learning objectives can be developed that reflect the institution's mission, the scope of the laboratory animal research projects, and the audience profile. In traditional academic settings, selected learning objectives would become the basis of test questions. In most adult education settings, the learning objectives are shared with course participants, who can use them to structure their learning experience or, after the course, to assess their retention of course content. Sample objectives or self-assessment statements are shown in Appendix III for the Core, Species-Specific, Pain-Management, and Surgery modules.

SCHEDULING THE COURSE

The frequency with which training programs are given and their scheduling depends on the total number of people who will receive training, the approximate number who will attend each session, and the availability of facilities and other resources. Mandatory training, which includes the core material required by federal regulations and institutional policy, is likely to be offered more frequently than are training opportunities for special topics or skill development. Offering multiple options for the dates and time of training will better enable scientists to participate with minimal disruption to their research and teaching efforts.

RESERVING FACILITIES

The training facility or facilities should be identified and evaluated before final scheduling is begun. Selection of a location convenient to the participants should be a primary consideration. The size of the room, the acoustics, and the lighting must be appropriate for the teaching format.

IDENTIFYING AND CONTACTING LECTURERS

Once the schedule is established and time is allocated for each content area, speakers for each segment of the program should be identified and contacted. The choice of speakers might include members of the laboratory animal resource staff; investigators with expertise in a topic area; members of the institutional animal care and use committee; and

personnel from public affairs, safety, or occupational health departments. Guest speakers might be desirable for certain topics. The selection criteria for speakers should include not only professional qualifications, but also their level of enthusiasm, oral presentation skills, commitment to the training effort, and ability to speak at the level of the participants.

OBTAINING AND REVIEWING AUDIOVISUAL MATERIALS

Audiovisuals are effective teaching tools and will help reinforce what is being said. Research has shown that people remember only 10% of what they hear, but will retain 50% of what they both *hear and see*. The materials and the equipment should be identified and reserved. The equipment must, of course, be compatible with the slides, videotapes, or films that are to be used.

All audiovisual aids should be previewed for content and technical quality. It may be appropriate to show only part of a film or slide program or to add slides to supplement the program. Slides or overheads should be uncluttered and easy to understand. It is better to use several slides than to crowd too much information on a single slide. Dark backgrounds and colors are more effective than are black on white.

Audiovisual resources can be borrowed from a number of sources, including the National Agriculture Library, the American Veterinary Medical Association, the American Association for Laboratory Animal Science, and the Foundation for Biomedical Research. Part IV furnishes more detailed information on ordering and purchasing audiovisual programs. In most instances, orders must be placed at least 4 weeks in advance.

ASSEMBLING REFERENCE MATERIALS

A large amount of information can be provided to participants as reference materials. These materials must be identified and ordered or duplicated. They might include sections from reference texts, institutional manuals, reprints, or copies of resources such as the *Guide for the Care and Use of Laboratory Animals* (NRC, 1985) and the *1986 Report of the AVMA Panel on Euthanasia* (AVMA, 1986). A bibliography has been provided in Part IV to assist in the selection of appropriate literature. Reference material should relate directly to course material presented to the participants.

PUBLICIZING THE COURSE

The program must be well publicized beginning approximately 6 to 8 weeks before the program is offered. This requires producing, duplicating, and mailing the announcement. Inclusion of all or part of the institutional commitment letter might encourage participation. A statement of the program's purpose and a brief outline of the topics and speakers should also be included.

Investigators should be asked to indicate which session(s) they plan to attend to ensure adequate seating and allow preparation of an appropriate number of handouts. Confirmation of attendance or program reminders should be distributed approximately 2 weeks before the program starting date.

REFERENCES

- AVMA (American Veterinary Medical Association). 1986. 1986 Report of the AVMA Panel on Euthanasia. *J. Am. Vet. Med. Assoc.* 188:252-268.
- Kemp, J. E., 1971. *The Instructional Design Process*. Belmont, Calif.: Fearon Publishers.
- NRC (National Research Council). 1985. *Guide for the Care and Use of Laboratory Animals*. A report of the Institute of Laboratory Animal Resources Committee on Care and Use of Laboratory Animals. NIH Pub. No. 86-23. Washington, D.C.: U.S. Department of Health and Human Services. 83 pp.

3

Evaluation

EVALUATING THE INSTITUTIONAL PROGRAM

Evaluation of a program charts progress toward institutional goals and also measures changes in attitudes and behaviors of the entire target population. To measure success in reaching the target audience, it is necessary to obtain baseline data, such as estimates of the size of the target audience at present plus estimates of the annual influx of new people. This information can be used to determine the percentage of the target audience who have participated in the education and training program.

Improvements in level of knowledge at an institutional level can be documented by comparing responses of groups that have attended courses with those that have not. It is important to gather baseline data before the first course is offered, as people who attend are likely to share information and demonstrate skills to others who have not yet attended, thus raising the knowledge and skill level for personnel taking subsequent courses. To evaluate success at an institutional level, course results should be compared with data obtained before the first course was given.

An attitude is an internal state that can be inferred from a behavior; therefore, attitudes can be measured by the choices an individual makes (Gagne and Briggs, 1979). To document changes in attitude, identify behaviors that indicate undesirable attitudes and behaviors that would result if attitudes were changed. For example, if an emphasis of the program is to increase cooperation between researchers and veterinary care staff, the number of contacts could be documented over a period of several weeks before the course is given and compared with the number of contacts after the course has been given. Other possibilities are to measure the number of people who attend education and training sessions voluntarily or changes in the use of animals. Consideration must be given to all

elements that will be measured. For example, if the comparison is between personnel voluntarily attending at the beginning of the education program and those voluntarily attending later, it must be remembered that with each course given, a smaller pool of untrained people may remain, and this pool will contain the personnel who are most resistant to participating in the program. Likewise, a simple change in the number or species of animals used may be a misleading measure, since animal use must correlate with the number and type of projects and the effectiveness of research data obtained.

EVALUATING THE COURSE

Courses should be evaluated routinely to monitor their effectiveness and identify those portions that require modification. Program participants should be surveyed immediately following each training session to gather specific information about the course organization and content and quality of instruction (see Table 2.1).

The methods and instruments used to elicit responses should be consistent, so that the training coordinator can use both historical and current information to evaluate programs and recommend changes. The most common method of evaluation is a check list of topics, with a choice of descriptive responses ranging on a scale from "1" to "10" (see Table 2.2). Statistical analyses usually require a variance of three points to distinguish differences in responses. Open-ended questions are more difficult to collate and quantitate but might provide insight that cannot be elicited from form questions. Forced-choice (yes or no) questions are often used, particularly when the questions involve value judgments or opinions.

A follow-up survey, conducted 6-12 months later, should be used to evaluate the impact training has had on the participant's planning and conduct of research, testing, and teaching (see Table 2.3). Qualified members of the laboratory animal medical staff may also observe actual research procedures that involve animal handling to ensure that the training has been effective and correct technique is being practiced. The institutional animal care and use committee might want to develop its own set of guidelines for evaluating the investigator's training and ability to conduct animal research.

REFERENCE

- Gagne, R. M., and L. J. Briggs. 1979. *Principles of Instructional Design*. New York: Holt, Rinehart, and Winston. 384 pp.

TABLE 3.1 Suggested Items for Immediate Course Evaluation

Course Organization**Allocation of time**

- Overall
- Individual sections

Content

- Appropriateness of level
- Applicability to job requirements

Individual Presentations**Quality of instruction for each major presentation**

- Preparation of speaker(s)
- Clarity and conciseness of presentation(s)
- Discussion encouraged
- Questions handled well

Effectiveness of format

- Lecture
- Audiovisual
- Printed materials
- Small-group discussions
- Wet-labs

Satisfaction with the Course

Which topic was most beneficial?

What changes would you recommend?

What topics should be added or deleted?

Would you recommend this program to your colleagues?

TABLE 3.2 Examples of Evaluation Instrument Form

Position and Job Category _____

Course Title _____ Date _____

	Strongly Agree	Strongly Disagree
The course was well organized.	1 2 3 4 5 6 7 8 9 10	
The time devoted to each topic was appropriate.	1 2 3 4 5 6 7 8 9 10	
The program content was appropriate for my job responsibilities.	1 2 3 4 5 6 7 8 9 10	
Instructor John Doe's material was well organized.	1 2 3 4 5 6 7 8 9 10	
Instructor John Doe presents the material well.	1 2 3 4 5 6 7 8 9 10	
I have a new level of understanding of the issues as a result of this course.	1 2 3 4 5 6 7 8 9 10	

TABLE 3.3 Examples of Items for Follow-up Course Evaluation

Position and Job Category _____

Course Title _____ Date _____

- Did the course help you to [for example] prepare animal care and use procedure statements?
- Did the course provide you with resources that were helpful in planning and conducting your research?
- What have you done differently as a result of this course?

APPENDIXES

I

Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training

U.S. Interagency Research Animal Committee

The development of knowledge necessary for the improvement of the health and well-being of humans as well as other animals requires in vivo experimentation with a wide variety of animal species. Whenever U.S. Government agencies develop requirements for testing, research, or training procedures involving the use of vertebrate animals, the following principles shall be considered; and whenever these agencies actually perform or sponsor such procedures, the responsible institutional official shall ensure that these principles are adhered to:

- I. The transportation, care, and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 et seq.) and other applicable Federal laws, guidelines, and policies.
- II. Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.
- III. The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.
- IV. Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain and distress in other animals.

V. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.

VI. Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.

VII. The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care shall be provided as indicated.

VIII. Investigators and other personnel shall be appropriately qualified and experienced for conducting procedures on living animals. Adequate arrangements shall be made for their in-service training, including the proper and humane care and use of laboratory animals.

IX. Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal research committee. Such exceptions should not be made solely for the purpose of teaching and demonstration.

II

The Animal Welfare Information Center

Kevin P. Engler and Jean A. Larson

ANIMAL WELFARE INFORMATION CENTER ESTABLISHED

In 1985, Congress amended the Animal Welfare Act (PL 99-198). This amendment authorized the establishment of an information service at the National Agricultural Library (NAL) that would, "... in cooperation with the National Library of Medicine, provide information (1) pertinent to employee training; (2) which could prevent unintended duplication of animal experimentation as determined by the needs of the research facility; and (3) on improved methods of animal experimentation, including methods which could reduce or replace animal use and minimize pain and distress to animals, such as anesthetic and analgesic procedures." The information service, established at NAL in 1986, was designated the Animal Welfare Information Center (AWIC). NAL houses 13 such information centers covering a variety of important agricultural topics.

Appropriations of \$750,000 per year for fiscal years (FY) 1987 and 1988 to fund the new information center were directed to the library through the Animal and Plant Health Inspection Service (APHIS). Funding for FY 1989 was added to NAL's base budget. The funding has been used to provide services to patrons, develop information products, purchase reference materials, and hire staff. Presently, the staff includes a coordinator and three technical information specialists.

SERVICES AND INFORMATION RESOURCES AVAILABLE THROUGH AWIC

NAL currently houses over 2 million volumes, including books, journals, newsletters, proceedings, reports, microforms, slides, videorecordings, films, and computer software. It

also coordinates a national information delivery network of state land-grant universities and USDA field libraries. The substantial resources of the NAL enable the AWIC staff to supply information on a broad array of subjects. Materials commonly accessed for AWIC's clientele cover important technical, ethical, political, and legal issues related to the welfare of animals. The publication *Animal Welfare Information Center Scope Notes for Indexers* outlines the animals and subject areas considered to be within the scope of the AWIC collection. Subjects that are indexed for use by AWIC include alternatives to the use of animals in research, testing, and education; euthanasia; analgesia; anesthesia; training and education of technicians and investigators; transportation and acquisition of animals; species husbandry; animal behavior; environmental factors affecting animals; laboratory animal management; institutional animal care and use committees; regulations and legislation concerning the humane treatment of animals; and philosophies of animal welfare or animal rights.

As directed by Congress, the AWIC staff emphasizes the acquisition of new materials related to the welfare of laboratory animals. Literature dealing with the welfare of farm animals and wild animals, however, represents a significant portion of the present NAL collection. Literature that involves the use of research animals as experimental units but does not address the welfare of the animals is generally not indexed. This type of information is collected by the National Library of Medicine. Also, because the Primate Information Center, University of Washington, has an extensive collection of primate-related materials, literature involving the use of laboratory primates is generally not indexed by NAL.

To access its extensive information resources, the NAL provides computerized bibliographic retrieval services through its in-house database Agricultural On-Line Access (AGRICOLA). This and other databases enable the staff to develop customized bibliographies tailored to the specific information needs of the patron. Established in 1970, AGRICOLA contains nearly 2.5 million citations covering aspects of agriculture and related subjects such as plant and animal production, food and nutrition, forestry, entomology, biotechnology, and rural development. While there is currently no database specifically for animal welfare, approximately one-fifth of the AGRICOLA database is devoted to citations on animal production, laboratory animal science, veterinary medicine, and animal welfare. AGRICOLA is currently available through the database vendors DIALOG Information Retrieval Service (in files 10 and 110) and the Bibliographic Retrieval Service (BRS)(in file CAIN), or commercially on compact disc. AGRICOLA/CAIN can be accessed from these vendors using standard dial-up computer terminals. The publication *Searching AGRICOLA for . . . Animal Welfare* details strategies and techniques for efficiently searching the database for animal welfare topics on both DIALOG and BRS. Other databases commonly utilized by the AWIC staff include the DIALOG files CRIS (60), MEDLINE (154,155), EMBASE (72,172,173), BIOSIS PREVIEWS (5,55), and CAB ABSTRACTS (50,53).

The staff also maintains vertical files of subjects and organizations related to animal care and use. These provide an excellent source of contact people and information about related organizations, as well as quick reference to current events and popular animal-related topics. The files contain records of acquisitions and clippings from current newspapers and magazines. They also include information about the history of animal welfare, legislation and guidelines pertaining to animal care and use, and organizations involved in

animal welfare or animal research. Other files are devoted to specific subject-related topics such as laboratory ferrets, computer simulations, guidelines for animal care in the United Kingdom, the Draize test, laboratory animal identification, and technician training.

The staff has developed an extensive network of subject experts and organizations active in the area of animal care and use. Referrals to individuals and groups may be provided on request.

A table-top exhibit describing the purpose and functions of AWIC is available for loan to interested groups. The display is sent by overnight mail, and copies of AWIC publications can be included. Return shipment must be arranged and paid for by the requestor.

AWIC services are available to USDA employees; federal, state or local government staff; academic and private institution staff; industry staff; students; and the general public. Under some circumstances, non-USDA personnel may be billed for services. Materials held in the collection can be obtained on interlibrary loan through institutional, business, academic, or public libraries. The information sheet *Document Delivery Services to Individuals* details the photoduplication and loan services to patrons for requested information. Information can be obtained by phone or mail request or by visiting AWIC in person.

AWIC REFERENCE PUBLICATIONS

To fill patron requests as quickly and thoroughly as possible, a number of bibliographic reference publications have been developed on specific topics in the area of animal welfare. These bibliographies address subjects that have been identified as critical animal welfare issues. For example, bibliographies are available on the Draize and LD50 tests, alternatives to the use of live animals for research and education, euthanasia, legislation, training materials for technicians and investigators, ethical and moral issues, transgenic animals, reference materials for members of institutional animal care and use committees, toxoplasmosis in laboratory animals, sources of simulation software, and laboratory animal housing and management. All AWIC bibliographies are distributed without charge. Many of these bibliographies are routinely updated to reflect new developments in each area, and efforts will continue to be directed toward developing new reference publications.

PROJECTS SUPPORTED BY AWIC

Since 1987, AWIC has supported a number of projects, either financially or through active participation, that promote the mandates of the Animal Welfare Act. The following projects were funded with grant monies provided by AWIC:

- An annotated bibliography of important literature relating to animal welfare entitled *Laboratory Animal Welfare Bibliography*, compiled by the Scientists Center for Animal Welfare (SCAW). (Available from SCAW and AWIC). An updated bibliography, also supported by AWIC, is in preparation.

- A handbook, partially funded by AWIC, produced by the National Research Council, Institute of Laboratory Animal Resources, entitled *Recognition and Alleviation of Pain and Distress in Laboratory Animals*.
- An educational videotape program, *Alternatives in Animal Research*, produced by Texas University Health Sciences Center, which will survey past and present ethical issues relating to animal research and discuss the concepts of reduction, refinement, and replacement in the context of experimental design and planning.
- Proceedings of a conference held June 22-25, 1988, by the Scientists Center for Animal Welfare (SCAW) entitled *Science and Animals: Addressing Contemporary Issues*, covering various aspects of animal experimentation. (Available for purchase from SCAW at \$25.00 per copy.)
- Two updated guidelines documents, *Laboratory Animal Management: Rodents* and *Laboratory Animal Management: Dogs*, to be produced by the National Research Council, Institute of Laboratory Animal Resources.
- Two publications on alternative animal toxicology testing methods entitled *Benchmarks: Alternative Methods in Toxicology* and *A Predictive Model for Estimating Rat Oral LD50 Values*, which were produced by the Princeton Scientific Publishing Company (Available for purchase from Princeton Scientific.)
- Twenty slide programs on care of animals to be produced by the American College of Laboratory Animal Medicine.
- Intelligence query assistance software in animal welfare produced by TOME Associates. (Available from AWIC.)

AWIC has also participated in formal cooperative agreements with several groups. The following joint projects have been implemented:

- An animal care training manual for principal investigators produced in collaboration with the University of Illinois at Chicago.
- Two reference volumes produced with the Agricultural Library of the University of Illinois at Urbana-Champaign entitled *Laboratory Animal Welfare Training Resource Directory* and *Laboratory Animal Welfare Research Guide*.
- An expert software system for anesthesia and analgesia in laboratory animals to be developed in association with the Central Animal Resource Facility of the University of Maryland.
- A videotape documenting normal and abnormal behavior of farm animals to be developed in association with Jack Albright, Purdue University.
- A Spanish language training videotape entitled *The Humane Care and Use of Laboratory Animals* to be produced in association with the Laboratory Animal Training Association.
- Publication of the proceedings of the SCAW-sponsored conference entitled *Agricultural Animals in Research*, which was held in September 1990.

Additional activities recently undertaken by AWIC, in cooperation with other groups, include:

- Distribution of *Chick Embryo Biology Information System (CEBIS)*, a bibliography prepared by John Bowen, University of Georgia, College of Veterinary Medicine.
- Establishment of guidelines with the National Library of Medicine for the cooperative acquisition of materials relating to animal welfare.
- Assumption of printing costs and distribution of the publication *Animal Care and Use in Behavioral Research: Regulations, Issues and Applications*. These proceedings of the invited papers session of the 1988 Animal Behavior Society meeting were prepared by the University of Colorado at Denver.

UPDATES REGARDING AWIC AND NAL

Patrons are welcome to visit AWIC and other NAL offices on weekdays from 8:00 am to 4:30 pm. A tour of the NAL facilities is available by appointment. For current updates regarding AWIC and NAL, the monthly newsletter *Agricultural Libraries Information Notes* is available free-of-charge. The Agricultural Library Forum (ALF), an electronic bulletin board system, also provides current information about new and existing products and services of AWIC and NAL and serves as a forum for the exchange of agricultural information between libraries, information centers, and other users. A "Brief Guide" to ALF has been prepared to introduce the major features of the system and to help callers get started.

For additional information please contact Animal Welfare Information Center, Room 205, National Agricultural Library, Beltsville, MD 20705 (301-344-3212).

PUBLICATIONS AVAILABLE THROUGH AWIC

Quick Bibliographies

- Animal Models of Disease (QB 89-07)
- Animal Welfare Legislation and Regulation (QB 89-23)
- Ethical and Moral Issues Relating to Animals (QB 89-03)
- Stress in Swine (QB 89-09)
- Welfare of Experimental Animals (QB 89-18)

Annotated Bibliographies:

- An Annotated Bibliography of Selected Materials Concerning the Philosophy of Animal Rights
- Laboratory Animal Welfare Bibliography (Scientist Center for Animal Welfare/National Agricultural Library)

Search Tip Series

- Searching AGRICOLA for . . . Animal Welfare (STS 88-01)

Special Reference Briefs

Alternatives to the Use of Animals in Research and Education (SRB 88-11)

Animal Care and Use Committees (SRB 89-06)

Animal Euthanasia (SRB 88-12)

Biotechnology: Methodologies Involved in the Production of Transgenic Animals (SRB 88-10)

The Draize Eye-Irritancy Test 1979-1988 (SRB 89-02)

The LD50 (Median Lethal Dose) Toxicity Test 1980-1988 (SRB 89-04)

Salmonella in Laboratory Animals (SRB 89-01)

Miscellaneous

ALF (Agricultural Library Forum): The National Agricultural Library's Electronic Bulletin Board System: A Brief Guide

The Animal Welfare Information Center Brochure

Animal Welfare Information Center Scope Notes for Indexers

Animal Welfare Information Center: Serials List

Animal Welfare Legislation: Bills and Public Laws 1980-October 1988

Animal Welfare Legislation: Bills and Public Laws November 1988-January 1989. Bills Submitted to the 101st Congress

Animal Welfare Legislation: February 1989-April 1989. Bills Submitted to the 101st Congress

Audio-Visuals in the Collections of the National Agricultural Library Relating to Animal Welfare

Reference Materials for Non-Affiliated Members of Animal Care and Use Committees
Training Materials in the Collections of the National Agricultural Library Relating to Animal Welfare

III

Sample Objectives or Self-Assessment Statements

INTRODUCTION

The following are samples of learning objectives or self-assessment statements that coordinators may want to use or adapt for use at their institutions. Additional statements should be developed as necessary.

CORE MODULE

Laws, Regulations, and Policies That Impact on the Care and Use of Animals

State the primary sources of regulations and policies affecting the care and use of laboratory animals.

State the major provisions of the Animal Welfare Act regulations and PHS policy.

Describe the composition and functions of the IACUC.

Outline the required contents of your institution's PHS Assurance Statements and annual reports to the USDA and the PHS Office for Protection from Research Risks.

Describe the possible penalties for noncompliance with federal regulations and policies.

Describe the policies of your institution that affect research protocols.

Ethical and Scientific Issues

Compare key elements of the deontological and the utilitarian positions on the use of animals in research, education, and testing.

List six ethical principles suggested in the U.S. government's Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training.
Discuss what you might do differently in the future in response to concerns over use of animals in research.

Alternatives

Define the "3R's".
Cite examples of nonanimal research methods and models that might aid you in your research goals.
Discuss how regulations and policies on the use of alternatives affect your present and future projects.
Cite the factors that influence animal model selection.
List services that you can use to gather information on alternatives and indicate how you have access to these services.

Responsibilities of the Institution, Animal Care and Use Committee, and Research and Veterinary Staffs

State three major institutional responsibilities.
List the mandated responsibilities of the IACUC.
Discuss how delegating authority to the IACUC provides protection to the institution, individual investigators, and research animals.
State six major categories of investigator responsibility and describe how these might be delegated among the principal investigator, co-investigators, and technical staff.
If your institution has policies relating to the major categories of institutional responsibility, state where copies of these policies can be obtained.

Pain and Distress

Define pain, stress, and distress.
State the principles of nonmalficence and beneficence.
Describe situations in which pain can be present when reflex responses are absent and absent when reflex responses are present.
Describe physiologic and behavioral signs that may indicate the presence of pain and distress.
Discuss steps taken by your institution in carrying out its legal obligations to minimize and control pain in animals.
Discuss the concept of adequate veterinary care as it relates to relief of pain.

Anesthetics, Analgesics, Tranquilizers, and Neuromuscular Blocking Agents

- Give an example of a pharmacologic agent that can produce each of the following: general anesthesia, analgesia, tranquilization, sedation, and chemical immobilization.
- List factors that are major determinants for calculating drug doses and drug effectiveness.
- List physiologic functions that should be monitored during general anesthesia.
- Describe how an anesthetic overdose is diagnosed, and what you would do if an overdose occurred.
- Describe requirements for recordkeeping associated with the use of pharmacologic agents, including special records required for procuring and storing controlled drugs.

Survival Surgical and Postsurgical Care

- Define major, minor, survival, and nonsurvival surgeries.
- Describe the facility and equipment requirements for performing survival surgery on rodents and on mammals other than rodents.
- Describe the major considerations for aseptic surgery.
- List the most common complications of survival surgery, and describe the environment and care that is necessary to prevent morbidity and pain.
- Describe in detail the records that must be kept for an animal on which a surgical procedure is performed.

Euthanasia

- Discuss the legal requirements for performing euthanasia on laboratory animals and cite the sources of laws, regulations, policies, and guidelines.
- List several examples of chemical methods of euthanasia and discuss the advantages and disadvantages of each.
- List several examples of nonchemical methods of euthanasia and discuss the advantages and disadvantages of each.
- Cite reasons for selecting the method of euthanasia that was chosen for use in your research protocol.
- Discuss ways in which professional and support staff may respond to the performance of euthanasia.
- Describe in detail your institution's protocol for disposal of animal carcasses, including any special considerations that may apply to your project.

Husbandry, Care, and the Importance of the Environment

- Discuss benefits to animal research derived from control of environmental variables.

Describe in detail the measures you have taken to ensure that the animals used for your research, teaching, or testing program are housed and cared for at all times in conformance with USDA regulations and PHS policy.

Describe the measures that will be taken to protect your animals in case of emergencies, such as a power failure.

Resources

Give examples of where you can find information regarding alternatives to use of animals.

Describe where you can find information on earlier studies related to your work.

Describe the resources available to you within your institution or community.

SPECIES-SPECIFIC MODULE

Selection and Procurement of Animals

For your specific project(s), discuss the reasons for your choice of animal(s) to be studied.

Discuss any legal requirements and institutional policies related to procurement of the animal(s) you have chosen for study.

Husbandry and Care

Discuss who is responsible for ensuring good husbandry practices and appropriate handling of the animals used in your project.

For the animals selected, state the size and construction materials of the cages you will be using, the population density that is appropriate, and the food- and water-delivery systems that will be used.

Discuss factors in the macroenvironment that are important to the particular species used in your research.

Animal Health

For the given species:

State normal physiologic parameters.

Describe physiologic and behavioral signs associated with pain and distress.

List the signs of common diseases or conditions that require veterinary intervention.

Safety and Health Considerations (Zoonoses)

For a given species, indicate routine precautions that should be taken to prevent transmission of disease.

State recommended precautions for handling known high-risk animals.

Specific Techniques

Assemble all instruments and material for performing a given procedure.

Indicate the structures or landmarks that will guide performance of the technique, including any structures that must be avoided.

State how you will know if the procedure is progressing as planned and how to respond to an error.

Euthanasia

Indicate the method of euthanasia to be used in a given project, and give the reasons for selecting that method.

**PAIN-MANAGEMENT MODULE
Definitions, Mechanisms, and Assessment**

Discuss the potentially painful aspects of your project and ways in which you will monitor subjects for pain and distress.

Legal and Ethical Obligations

Discuss what you are required to do to meet your legal and ethical obligations.

Discuss how the attending veterinarian can assist you.

Alleviation of Pain or Distress

Suggest several ways that research staff and caregivers can reduce pain and distress in research animals without using pharmacologic agents.

Give examples of situations in which you might choose to use a tranquilizer, an analgesic, or a neuromuscular blocking agent.

For a specific animal and drug, calculate dosage and give details of administration.

Explain "dosage to effect" for anesthetics, and list factors that influence effectiveness.

Anesthetics

Write out instructions for preanesthesia, initial dose of anesthetic, and follow-up dosage, as necessary, specifying time intervals and methods of monitoring effectiveness. Describe signs of overdose, and state what interventions you would initiate.

Euthanasia

Discuss conditions under which you would be required to kill an animal before completion of the experiment and the procedure you would follow.

SURGERY MODULE

Legal Requirements for Survival Surgery

Write a proposal for survival surgery on the species of your choice, providing sufficient information to demonstrate compliance with legal and institutional requirements.

Aseptic Technique

For a specific procedure on the species of your choice, describe in detail all areas of preparation for aseptic surgery, indicating who on the surgical team is involved in each action.

Selection and Administration of Anesthetic

For a specified animal and surgical protocol, write a pain-management protocol, stating dosage and assessment of effectiveness.

Animal Monitoring

For a specified animal, give the range of vital signs that you would consider acceptable during the surgical procedure and methods of monitoring vital signs during and immediately after surgery.

Surgical Techniques

Describe the surgical procedure(s) you are using in your research, including equipment and instruments needed.

Describe the suture material preferred for the surgical procedure of your choice and state what precautions you would take to prevent dehiscence and infection.

Postsurgical Care

For a specific animal and a specific procedure, write a protocol for routine postsurgical monitoring, including indicators of when the animal can be returned to normal caging. Describe the signs of shock and state what interventions you would initiate in the presence of these signs.

Medical Records

List and describe all pertinent and required items that should be entered into the medical record of an animal subjected to surgery.

Terminal Surgeries

For a given animal, elect a method of euthanasia and indicate the exact procedure, including confirmation of death, and disposal method that you would use.

EDUCATION AND TRAINING IN THE CARE AND USE OF LABORATORY ANIMALS A Guide for Developing Institutional Programs

Federal law now requires that institutions provide training for anyone caring for or using laboratory animals. This volume provides the guidelines and resources needed to coordinate a quality training program, as well as to meet all legal requirements. **Education and Training in the Care and Use of Laboratory Animals** provides content information for required topics—from ethics to record keeping—and lists sources of additional publications, audiovisual programs, and computerized teaching aids. It includes ready-to-use teaching outlines, with detailed instructions for presenting material; practical guidelines on logistics covering scheduling, budgeting, and more; and directions on how to design training for adults and how to work with investigators who might resist taking training courses. This practical guidebook will be necessary for research institutions, particularly for staff members responsible for training coordination.

Also of interest . . .

IMMUNODEFICIENT RODENTS A Guide to Their Immunobiology, Husbandry, and Use

This volume is an indispensable reference on the nature of immune defects in rodents and the special techniques necessary to maintain and breed them. The authors describe 64 inbred, hybrid, and mutant strains of rodents, each with some immune defect; explain mechanisms for ensuring genetic purity; and provide a standardized nomenclature for different varieties. Subsequent sections summarize and provide references on the genetics, pathophysiology, husbandry, and reproduction of each of the various strains as well as sound advice on planning for the selection, transportation, housing, and maintenance of these animals.

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